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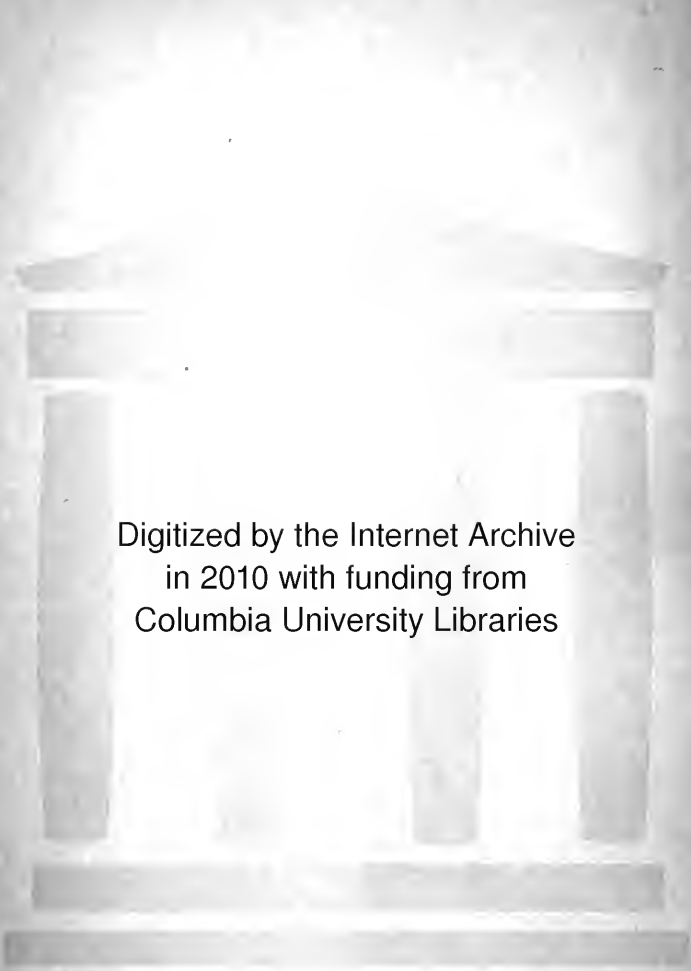


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PHYSIOLOGICAL ASPECTS
OF
THE LIQUOR PROBLEM

INVESTIGATIONS MADE BY AND
UNDER THE DIRECTION OF

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SUB-COMMITTEE OF THE COMMITTEE OF FIFTY TO
INVESTIGATE THE LIQUOR PROBLEM

VOLUME II



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A CRITICAL REVIEW OF THE PHARMACOLOGICAL ACTION OF ETHYL ALCOHOL,

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CONSTITUENTS OF ALCOHOLIC
BEVERAGES.

By JOHN J. ABEL, M. D.



A CRITICAL REVIEW

OF THE

PHARMACOLOGICAL ACTION OF ETHYL ALCOHOL.

I. A STATEMENT OF THE RELATIVE TOXICITY OF THE CONSTITUENTS OF ALCOHOLIC BEVERAGES.

1. GENERAL CONSIDERATIONS.

FROM a physiological point of view the alcohols are not agents having an action peculiar to themselves. There are many compounds which belong to the methane series whose action presents numerous points of similarity. Such are to be found among the hydrocarbons of a low boiling point, as ligroin; among the ethers and mixed ethers, as ethyl ether and methyl propyl ether; among the esters, such as acetic ether; among the ketones, pinnakones, aldehydes, and their derivatives; among the amides of the fatty acids, the halogen substitution products of hydrocarbons, the sulphides, and mercaptans. Also among the so-called aromatic compounds there are several classes, such as the phenols, the amides of acids, and the terpenes, whose action on the brain in large doses bears more or less resemblance to that of large doses of ethyl alcohol.

From a sociological and hygienic point of view, ethyl alcohol is the most important of the alcohols. It was clearly set forth many years ago by Lallemand, Perrin, Marvaud, Richardson, and other writers, that this alcohol acts on the higher nervous centres in a manner similar to that of the anæsthetics and hypnotics. Well-known examples of the latter substances are ether, chloroform, chloral, amylene hydrate, paraldehyde, and sulphonal.

An exhilarating action is an inherent property of these substances in certain doses. Occasionally the physician meets with

persons who have formed the habit of inhaling chloroform from the palm of the hand or from a lightly saturated handkerchief. The inhalation is usually carried on for a short time only, and its object is to induce a pleasant form of mental stimulation. Only occasionally is the inhalation of chloroform carried on until helpless intoxication occurs.

It is also well known that ethyl ether, the ordinary agent employed among us to induce surgical anæsthesia, may serve the purposes of an intoxicant. The so-called "ether frolics" which were often indulged in by parties of young people in the days of the itinerant lecturer on laughing gas and ether illustrate this point. Further proofs are found in the extent to which ether drinking was at one time practiced in parts of Ireland and Norway. Very recently this habit has assumed such proportions in southwestern Russia that the physicians of the district have petitioned the central government at St. Petersburg to interfere in the matter. It seems that the practice has arisen in consequence of the conversion of the sale of vodka into a state monopoly in order to check drunkenness.

With the increasing development of organic chemistry, the number of substances capable of acting as speedy intoxicants will, no doubt, greatly increase.

That alcohol can induce as profound an anæsthesia as any of the substances named is also well known. In the days before anæsthesia it was the custom of bone setters to ply their patients with alcohol in order to facilitate the reduction of difficult dislocations. Extreme muscular relaxation and insensibility to pain were thus induced. Capital operations have been performed with the help of whiskey, and even in our own time a few have proposed that alcohol should be substituted for the usual anæsthetics of surgery. The anæsthesia produced by alcohol is, however, not commendable, since it cannot safely be induced in a short time and is too prolonged. The quantity needed for surgical anæsthesia would in many cases lead to a fatal result.

2. ON THE RELATIVE TOXICITY OF SEVERAL ALCOHOLS, ALCOHOLIC BEVERAGES, AND THEIR CONSTITUENTS.

Before entering upon a detailed account of the physiological action of ethyl alcohol, it will be advisable to consider

briefly what part of the action of alcoholic beverages is to be ascribed to the several alcohols contained in them, what part to other constituents, and especially what degree of toxicity is to be attributed to ethyl alcohol, — their chief constituent. These questions are of great importance from the point of view of hygiene and have an important bearing on legislative enactments.

In speaking of the toxicity of an agent so widely employed as is alcohol, it should be borne in mind that the terms poison and toxicity are here employed in a scientific sense. According to scientific usage any substance is called a poison which, when incorporated into the blood, or even when applied to the mucous membranes and other surfaces, in relatively small amounts, causes disturbance in any function of the body. It is difficult to give a satisfactory definition of a poison.

Without entering on a long definition of the term, we may remark that, without exception, all poisons are capable of being taken without *demonstrable* injury in a certain quantity, which is, for each of them, a special though sometimes very minute fraction of their toxic or fatal dose. There is no substance which is always and everywhere a poison. The term is relative: conditions and circumstances of various kinds must always enter into the conception of the term. No one would maintain, for example, that a cup of delicately flavored tea is in any sense injurious or poisonous to the average healthy adult. And yet caffeine, the active principle of this cup of tea, is a poison as surely as is alcohol. When used in a strictly scientific sense, the term applies with equal propriety to a number of other food accessories, as coffee, pepper, ginger, and even common salt. In this last instance the toxic dose is large. The Chinese are said to make use of common salt now and then for committing suicide. A half teacupful of it, made into a mush with a little water and swallowed perforce on an empty stomach, will set up such an inflammation of the gastro-intestinal tract that death may follow. The too sweeping and unrestricted employment of this term in reference to alcoholic beverages immediately meets with the reply that if alcohol be a poison it is indeed a slow poison, since many have used it in moderation up to old age with apparently no prejudicial effects on health.

During the past fifty years two opposing views have been

held as to the relative toxicity of the constituents of alcoholic beverages.

One class of investigators has ascribed a large share of the physical evils of drunkenness to the higher alcohols and other by-products of alcoholic beverages, and has insisted on the great importance of the enactment of laws guaranteeing the manufacture of "pure" alcoholic beverages. These investigators have been wont to claim that the prohibition of the sale of adulterated and made liquors, coupled with a system of high license, would practically solve the drink problem. A second class of investigators has maintained that it is illusory to hope for any perceptible lessening of the drink evil in consequence of the passage of laws which shall insure "pure" alcoholic beverages. While admitting that such laws are desirable on hygienic grounds, just as they are in relation to other food accessories and table luxuries, they maintain that these laws fail of reducing intemperance for the reason that ethyl alcohol, which is the chief constituent of all alcoholic beverages, is in itself capable of producing all of the symptoms and lesions of chronic alcoholism. According to this view the impurities contained in even the poorest grades of whiskey, etc., are quantitatively insignificant as compared with ethyl alcohol and play only a secondary rôle in the whole train of evils due to chronic alcoholism. In a word, according to this school, the drink evil is nothing but the misuse of ethyl alcohol.

These opposing views have led to numerous researches on the chemical composition of alcoholic beverages and on the toxicity of the various substances contained in them. To give a detailed account of all the work that has been done in these fields would require a volume; and we can give here only a brief outline such as will make our conclusions intelligible.

The numerous products found in "pure" alcoholic beverages, aside from water and ethyl alcohol, may be classed under the following heads: aldehydes, esters (ethers), higher alcohols, acids, basic products, terpenes, glycerine, sugar, albumens, extractives, coloring matters, fats, and mineral constituents. These various by-products which arise in the course of alcoholic fermentation, and which undergo various modifications during the ripening of alcoholic beverages, give commercial value to these beverages. Old cognac, whiskey, and fine old wines owe their

agreeable taste and odor, and consequently their high price, solely to the small quantities of higher alcohols, esters, aldehydes, etc., which they contain.

Ethyl alcohol, diluted with water until it equals the alcohol content of whiskey or wine, forms a somewhat less toxic mixture than the most valued of the natural beverages; but it has only a low commercial value on account of its indifferent taste and odor. The alcohol question would not have reached its present dimensions had not nature mingled with ethyl alcohol a host of sapid substances, which give each alcoholic beverage its separate character and account for the estimation in which it is held.

Adulterated and artificially prepared beverages may contain substances not belonging to the classes just enumerated, as, for example, other esters or "bouquets," other coloring matters and preservatives, such as salicylic acid, boracic acid, or sulphites.

No sharp distinction can be drawn between adulterated and artificially prepared products, unless we restrict the application of the term to such as contain one or more substances not actually found in alcoholic preparations. It may safely be asserted that adulteration in this sense is of less frequent occurrence than is the artificial production of cognacs, liqueurs, etc., which are so skillfully compounded as to contain the same constituents as are found in natural beverages having the same names.

In the popular mind no distinction is made between varieties of spurious drinks, and the impression prevails widely that spirituous liquors, wines, etc., are more or less adulterated, drugged, or "made up," and that the adulterants present often produce worse effects than the alcohol itself.

In regard to this point I cannot do better than to cite the Reports of the Laboratory of the Inland Revenue Department of Ottawa, Canada, of the year 1891, in which Chief Analyst Macfarlane expresses himself in the following words: "In general it may be remarked that the adulterations detected consisted for the most part of dilution by water and the addition of coloring substances not injurious to health. None of the substances enumerated in the first schedule of the Adulteration Act were found in any of the samples, with the exception of occasional traces of amyl alcohol (fusel oil). Diligent search

for methyl alcohol (from the possible addition of methylated spirit) failed to discover any."

These statements summarize Macfarlane's conclusions with regard to 680 samples of distilled liquors collected from retail dealers in different cities of Canada. Of these 680 samples 102 were found to be adulterated in the sense above described, 26 were classed as doubtful, and 552 were classified as being unadulterated. Macfarlane goes on to say that "in the course of the discharge of their duties the officers of this branch have become aware that among the various brands of distilled liquors offered for sale in Canada there are many of spurious character, not derived from the source indicated by their names, and, in fact, as stated in the newspaper extract above quoted, made up of alcohol, water, and other materials. It was, however, found to be a difficult matter to distinguish the factitious from the genuine article, and no attempt in this direction appears to have been made by any of the public analysts. In fact, the existence of this sort of manufacture has long been known to, and recognized by, the Inland Revenue Department, but it is only recently that the various ethers, essences, and oils used in the production of spurious brandy, rums, gin, whiskey, etc., have been publicly offered for sale. This branch is, however, not yet in possession of any information to show that any advantage has been taken of these facilities by retailers, to any very large extent, to manufacture brandies, etc., on their own premises."

Macfarlane says that his investigation leads generally to the following conclusions: "(1) That the opinion held by many regarding the injurious character of the substances added to spirits or distilled liquors for various purposes is destitute of sufficient foundation. Some of the essences, ethers, etc., used by blenders or compounders, taken by themselves, may be said to be injurious, but the quantities used are so minute in the resulting product that they cannot be considered to have any worse effect on the human system than the dilute alcohol with which they are mixed. (2) That in very many cases liquors are sold under the description of brandy, rum, Scotch and Irish whiskey, and gin which have no right to such names, on account of their being merely imitations. (3) That this branch finds it impossible, under the Adulteration Act, to prevent such

sale until the limits of variability have been fixed and standards established by the Governor in council or by Parliament."

Mr. Samuel P. Sharpless, the State Assayer of Massachusetts, has lately said: "The whiskies examined in Massachusetts, as a rule, have been free from any substance more injurious than the alcohol they contain. They have generally (as well as the other distilled liquors examined) been of standard strength—that is, they have contained about fifty per cent. of alcohol and as a rule have not given much over the amount of residue allowed by the Pharmacopeia. . . . Large amounts of rectified spirits are used in the preparation of whiskies for the market, where the whiskey is used only as a flavoring material. But such manufactured whiskies meet the requirements of the Pharmacopeia better than the genuine article, being more free from the higher alcohols and ethers than is pure whiskey. The only point in which they do not agree is that they are not three years old. But the only method for determining the age of a liquor that I am acquainted with is the brand on the barrel. It certainly cannot be determined by any chemical means."

My own very limited experience in the analysis of alcoholic beverages would lead me to accept the above statements of the analysts just cited. Thus I have recently examined a specimen of whiskey which is retailed to the colored people and poorer whites of Washington, D. C., at fifteen cents a pint. It contained thirty-seven per cent. by volume of ethyl alcohol, was almost entirely free of fusel oil, and owed its color to burnt sugar. It was undoubtedly made by the simple process of adding water and burnt sugar to the ordinary ethyl alcohol sold by Western distillers.

The analysts of European countries have also found that adulterated and artificially prepared beverages often approach so closely in composition to the analogous natural products that even skilled chemists cannot distinguish between the two classes. This is true especially of artificial cognacs and liqueurs. It is only the skilled connoisseur in the taste and odor of these liquors who can detect a difference in quality. Even when inferior "wine oils" and essences are employed in their manufacture, such, for example, as contain balsam of Peru (cinnamic and benzoic acids), it is more than probable that the chemist will overlook these unnatural by-products. Dr. Snell, of the

German Imperial Health Office, has pointed out that one litre of a cognac essence may contain twenty grams of Peru balsam. One litre of this essence will yield, when mixed with the appropriate quantity of spirit and water, one hundred litres of artificial cognac, and the finished product will therefore contain only 0.02 per cent. of Peru balsam, which will not be detected unless very large quantities of the cognac are worked up by the analyst.

This instance is cited to show how difficult it may be to detect a spurious article. The Peru balsam in these quantities is not a dangerous by-product, — not as much so as others present in cognacs made by the usual processes. As a rule the artificial cognacs of France compare well with the natural product in respect to their content of higher alcohols, etc.

Where state supervision is lax, flavoring products, coloring matters, etc., more harmful than those found in natural beverages are no doubt often introduced. One of the chief dangers lies in the introduction of an excess of the higher and more toxic alcohols when badly rectified spirit is used in making up a spurious article. As we shall see, the toxicity of an alcoholic beverage increases rapidly with an increase in the percentage of the "fusel oil" or higher alcohols.

Legislation which requires a certain standard for all alcoholic beverages is demanded in the interests of public health, entirely aside from the point as to how it affects the question of intemperance.

The term "fusel oil" is applied by some analysts to the sum total of those impurities in whiskey, etc., which come under the heads higher alcohols, ethers, and aldehydes; others include even more under the term, while a few apply it only to the sum of the higher alcohols. From the toxicological and medical point of view the higher alcohols, aldehydes, and ethers are the only by-products in spirits worth considering — at least in those that are made by the usual processes.

In "pure" wines the various ethers and aldehydes constituting the "bouquet," the degree of acidity, the amount of sugar and salts, are of importance both from a medical and from a hygienic point of view. When the wines are adulterated or when they are made artificially, the harmful action of poisonous coloring matters, of lime salts, and of alum must

be taken into account. In regard to the malt liquors it may be said that the by-products of the well-made varieties are of little consequence, except when enormous quantities are consumed. In such cases a great burden is thrown upon the organs of excretion, not only to rid the body of the salts, extractives, etc., but also of the large excess of water taken up. That beer in great excess is harmful to the kidneys and heart and other organs has been proved by the researches of medical authorities in Munich and other German cities. The alcohol contained in it is the main cause of injury, yet it is not its only harmful constituent when it is taken in great excess. The question of adulteration is also of importance here.

The more concentrated alcoholic liquors or spirits are, from a practical point of view, the most toxic of all alcoholic beverages. This is due solely to the fact that they are consumed without first being diluted. If whiskey or cognac were always to be diluted with water until the percentage of alcohol was brought down to ten per cent., they would be no more toxic than wine of the same strength. In fact, a number of French authorities maintain that the finest wines are, in proportion to the amount of alcohol contained in them, more toxic than the brandies. The question of the relative toxicity of the various constituents of alcoholic beverages has been narrowed down to a study of the action of the higher alcohols, the ethers, and aldehydes as compared with that of ethyl alcohol. This point of view is justified for the stronger beverages, such as the liqueurs, brandy, rum, whiskey, etc., and the stronger wines. As we have seen, however, a study of the misuse of beer would have also to take account of other factors. As these factors have not yet been made the object of special study, we shall confine ourselves to the by-products found in spirits and wines.

Analysis shows that a litre of rum contains on the average about

500 c. c. of ethyl alcohol,
0.763 c. c. of ethers,
0.153 c. c. of aldehydes,
0.034 c. c. of furfural,
0.387 c. c. of higher alcohols.

The ethers, aldehydes, furfural, and the higher alcohols together amount to 1.337 c. c. in the litre, or less than $1\frac{1}{2}$ parts

by volume in the thousand. In most brandies the sum of these constituents amounts to less than two grams in the litre. According to the analyses of Riche, their sum rarely reaches three to four grams, and only in exceptional cases five to six grams, in the litre. The whiskies also contain far less of these deleterious products than was once thought to be the case. Windisch, of the Imperial German Health Office, analyzed a large amount of whiskey especially prepared from pure, selected rye. The amount taken yielded by distillation 12,532 litres of absolute alcohol and only sixty-one kilograms, or 73.22 litres, of "fusel oil." If we assume that the original whiskey was of average strength, the amount used in the experiment must have exceeded 25,000 litres. Each litre, therefore, contained less than three grams ($\frac{1}{10}$ oz.) of the harmful fusel oil, — that is, less than this small amount of higher alcohols, aldehydes, and esters combined.

Spirits made from grains, contain as a rule a larger percentage of the higher alcohols than equally good specimens of potato spirit. Some of the poorest specimens of rum and raw whiskey are found to contain little more fusel oil than the good specimens. Raw spirits may, however, contain traces of substances not found in better spirits, which affect their taste if not their physiological action. Thus, small quantities of paraldehyde, of allyl alcohol, collidine, hydrogen sulphide, etc., have been found in raw spirits.

It has been stated that artificial and made spirits do not, as a rule, contain more of the higher and toxic alcohols than natural products. This appears to be true of foreign countries. Numerous analyses have been made in France and Germany which prove this point. In illustration the following table, which is taken from Daremberg, is offered:—

	Old cognac natural.	Artificial cognac.	Armagnac 3 years old.	" Made " armagnac.
Acids	0.600	0.060	0.468	0.084
Aldehydes	0.106	0.001	0.063	0.031
Furfurol	0.006	0.000	0.007	0.002
Ethers	0.422	0.080	0.360	0.088
Higher alcohols	0.800	0.034	0.810	0.021
Total	1.934	0.175	1.708	0.226

	Jamaica rum.	"Made" rum.
Acids	1.224	0.384
Aldehydes	0.154	0.018
Furfurol	0.021	0.002
Ethers	3.080	0.194
Higher alcohols . .	0.653	0.058
Total	5.132	0.656

The sum total in each column represents the amount, in grams, of the constituents enumerated, which is found in one litre of the cognac or rum tested.

Among the higher alcohols amyl alcohol preponderates; among the aldehydes furfurol is the only one worth considering. Amyl alcohol, as a rule, is present in the proportions of less than one half part in the thousand; the ethers of various kinds hardly ever, except in certain wines, amount to more than 0.7 part in the thousand; while furfurol is present, on the average, in such small amounts as fifteen to forty milligrams in the litre.

Even the more harmful alcoholic beverages, therefore, contain only a small percentage of dangerous and intoxicating substances other than ethyl alcohol. Exception need only be made for some of the grosser and adulterated products, which may contain a little methyl or allyl alcohol in addition to one half per cent. of the higher alcohols.

Ethyl alcohol is present in all spirits somewhere in the proportion of fifty per cent. by weight. In wines it may vary to the extent of from seven to twenty-three per cent. by weight if "fortified" wines are included. It is evident, then, that the by-products would have to be extremely poisonous in comparison with ethyl alcohol in order to play a rôle of any importance in either acute or chronic alcoholism.

3. TOXICITY OF THE CONSTITUENTS OF ALCOHOLIC BEVERAGES.

Ethyl alcohol is only a weak poison for all organisms. Loew and his pupils have shown that algæ can withstand the effects of a two per cent. solution for twenty-four hours; molds tolerate a solution containing as much as four per cent., but show its effect in hindrance of growth. It requires, however, a ten per cent. solution to damage them seriously and permanently. Infusoria tolerate a one per cent. solution for some time, and

many species of algæ live in a solution of this strength for several days.

Dubois has shown that sea anemones show no signs of derangement when they are placed in sea water containing one per cent. of alcohol. Where the water contains two per cent. they begin to be affected, their tentacles are withdrawn, and the entire body is contracted into a small volume. They are still sensitive to touch and respond to the stimulus of weak electric currents. Even after remaining for twenty-four hours in a five per cent. solution, recovery takes place when they are put into fresh sea water.

The higher alcohols are more toxic than ethyl alcohol for lower as well as for higher forms of life. Thus, isopropyl alcohol, $\text{CH}_3\cdot\text{CH}\cdot\text{OH}\cdot\text{CH}_3$, butyl alcohol, $\text{CH}_3(\text{CH}_2)_2\cdot\text{CH}_2\cdot\text{OH}$, isobutyl alcohol, $(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2\text{OH}$, and tertiary butyl alcohol, $(\text{CH}_3)_3\text{C}\cdot\text{OH}$, in two per cent. solution are tolerated by *spirogyra* for some time. The formation of starch is not, however, observed to go on in solutions of this strength.

It will be brought out more clearly in a later paragraph that the primary, saturated alcohols of the series $\text{C}_n\text{H}_{2n+1}\text{OH}$, increase in toxicity in an ascending degree from the first two members of the series, methyl and ethyl alcohol, on upward through propyl, butyl alcohol, etc.

The experiments of Bokorny also show interesting physiological relations in respect to the behavior of the polyvalent alcohols. Thus, while ethyl alcohol, $\text{C}_2\text{H}_5\text{OH}$, is a weak poison for algæ, the corresponding dihydric alcohol, ethylene glykol, $\text{CH}_2\cdot\text{OH}\cdot\text{CH}_2\cdot\text{OH}$, is a good nutrient for these plants. Propyl alcohol, $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$, is also a relatively weak poison for algæ, while the corresponding trihydric alcohol, glycerin, $\text{CH}_2\cdot\text{OH}\cdot\text{CH}\cdot\text{OH}\cdot\text{CH}_2\cdot\text{OH}$, is an admirable source of carbon for them and even for higher plants. The introduction of additional hydroxyl groups into alcohols of the fatty series appears, therefore, to give to them a more decided nutritive and a lessened narcotic quality.

Tsukamoto, a pupil of Loew's, has also shown by extensive experiments on higher and lower plants and on various aquatic forms, such as infusoria, ostracodes, and tadpoles, that the toxic action of the alcohols of the methylic series runs parallel with the number of carbon atoms in their molecule; that is, with the

increase in molecular weight. While one per cent. solutions of methyl and ethyl alcohol had no effect on algæ, germinating seeds of barley, the soya bean, swedish turnip, etc., or on the lower aquatic forms (cyprus, cypridina, and infusoria), propyl alcohol of this strength was fatal to all in three days; 0.5 per cent. solutions of normal butyl alcohol killed algæ in three days, 0.5 per cent. solutions of isobutyl alcohol in four days, and tertiary butyl alcohol in the same strength required longer. 0.5 per cent. solutions of amyl alcohol killed them in one day. Amyl alcohol in 0.1 per cent. solution killed all the ostracodes and many infusoria in one day. In 2 per cent. solutions ethyl alcohol acted more rapidly than methyl alcohol, but even in this strength it required five days to kill all the cells of *spirogyra*.

The primary unsaturated alcohol ($\text{CH}_2:\text{CH}\cdot\text{CH}_2\cdot\text{OH}$),—known as allyl alcohol,—was the most poisonous alcohol examined. Germinating seeds, microbes of putrefaction, and *spirogyra* were killed in less than twenty-four hours by solutions of 0.5 per cent. of this alcohol. It required a two per cent. solution of amyl alcohol and a twenty per cent. solution of either methyl or ethyl alcohol to have the same effect on the putrefactive microbes. Infusoria and ostracodes were killed by allyl alcohol in twenty-four hours, even when the solution contained only 0.005 per cent. It required a five per cent. solution of amyl alcohol to act with equal intensity.

That the unsaturated allyl alcohol is also exceedingly poisonous for higher animals has been shown by Meissner's experiments on mice and rabbits. So small a quantity as 0.1 c. c., when injected subcutaneously, killed a rabbit in two and one half hours, and when given by the stomach it killed the animal in nine hours. This alcohol lacks the narcotic property, but is a powerful irritant for mucous surfaces, greatly depresses the entire circulatory apparatus, and causes convulsions and respiratory paralysis.

Many observers have shown that lower vegetable forms can utilize the less toxic alcohols in building up the proteids or cellulose of their cells. The availability of the alcohols for this purpose varies greatly. While methyl alcohol can be utilized in concentrations of one per cent., amyl alcohol must be diluted to 0.1 per cent. before it will serve as a nutrient.

Duggan has made a study of the influence of the alcohols on

the conversion of starch by diastase. While we are not dealing here with a vital action, it is nevertheless of interest to note that here too the activity of the primary alcohols increases with the addition of each CH_2 group. Ringer and Sainsbury have found that the primary alcohols form an ascending series in regard to their poisonous effects on the frog's ventricle. The toxicity of the series may be represented by the following numbers, which indicate the relative amounts required to paralyze the heart:—

Methyl alcohol	205.5	Butyl alcohol	17
Ethyl “	114	Amyl “	6.6
Propyl “	59.3		

Rabuteau's experiments, made on frogs which were immersed in water containing varying proportions of primary alcohols, also prove the greater toxicity of the higher numbers of the methylic series. Amyl alcohol was found to be fifteen times as poisonous as ethyl alcohol and three or four times as poisonous as butyl alcohol. According to Rabuteau, these results have been substantiated by Dogiel. The more recent investigations of Picaud also corroborate these assertions.

This investigator experimented on birds, on specimens of the batrachian known as *Triton vulgaris*, and on the ordinary gold-fish (*Carrassius auratus*). The last-named animal reacted in the following manner to ethyl and amyl alcohol. When the water into which it was put contained three parts in the 100 of ethyl alcohol it died in ten hours; when it contained four parts in the 100 it died in two hours; when it contained eight parts in the 100 it died in one hour; when it contained twenty to twenty-one parts in the 100 it died instantly.

Of amyl alcohol it required only 0.1 part in 100 parts of water to kill it in one and a half hours, only 0.2 in the 100 parts to kill it in one half hour, and 0.5 parts in the 100 to kill it in eight or nine minutes. Picaud draws up the following scale of toxicity for the alcohols tested by him, the toxicity of ethyl alcohol being put at 1.

Methyl alcohol	$\frac{2}{3}$	Butyl alcohol	3
Ethyl “	1	Amyl “	10
Propyl “	2		

Many experiments have been made which prove that the higher animals in general are affected in the same way by the

higher alcohols. Hemmeter has shown that the working power of the dog's heart is greatly reduced by the higher members of the methylic series. The reductions in the amount of blood pumped round by the heart in thirty seconds under the influence of one fifth of one per cent. in the blood of each of the several alcohols are represented by the following numbers : —

Methyl alcohol	19.46 c. c.	Butyl alcohol	161.121 c. c.
Ethyl "	17.45 "	Amyl "	322.32 "
Propyl "	79.705 "		

If we take only the heart into account, amyl alcohol would be more than eighteen times as poisonous as ethyl alcohol, a result which agrees closely with the figures given by Joffroy and other French observers. According to Hemmeter, methyl alcohol is more poisonous than ethyl alcohol. Warren has shown that if Hemmeter had expressed the diminution in output in percentages of the normal amounts of blood pumped out by the heart, the following series of figures would have been obtained, as expressing the relative increase in toxicity from methyl to amyl alcohol : —

11.4, 15.5, 47.2, 83.4, 199.

In this method of expressing Hemmeter's results methyl alcohol is less toxic than ethyl alcohol and falls into the place which all the later experimenters assign to it.

More frequently investigators have expressed the relative toxicity of a series of alcohols in terms of a series of numbers which express the quantity required to kill one of the higher animals inside of twenty-four or forty-eight hours. There has been much discussion as to which species of animal most nearly approximates to the human being in its resistance toward alcohol, also as to the best method of administering the alcohol, whether by intravenous injection or by the stomach, as to the influence of the speed of injection in the intravenous method, and other technical points which cannot be taken up here. The French literature of this subject contains many discussions bearing on these technical details. The writings of Joffroy, Daremberg, Dujardin, Laborde, Magnan, and others, may be consulted by those who care to examine the technical points involved.

All experiments of the kind now to be described, whether made on dogs, rabbits, pigs, guinea pigs, cats, birds, etc., are

made with the object of determining for each alcohol its *toxic equivalent* in acute poisoning. Bouchard defined this term as signifying the amount of alcohol capable of killing one kilogram of animal inside of about twenty-four hours. Later workers, as Joffroy and his pupils, have distinguished between the *true toxic equivalent* of acute poisoning and the *experimental toxic equivalent*. The latter represents the quantity (per kilogram of body weight) actually injected, and it is always somewhat larger than the amount actually required to kill the animal inside of twenty-four or forty-eight hours.

The results of various experimenters are not always in close agreement. This is not astonishing when it is remembered that widely different methods have been employed by the several experimenters. Thus, some of the earlier investigators, as Dujardin, generally used the subcutaneous method of administering the alcohol, others made use of the stomach, and still others of the veins. G. Baer, in a recent paper, gives the following numbers for the toxic equivalents of the first five alcohols of the methylic series, as tested by injection into the stomach of the rabbit.

	Toxic equivalent, or grams of alcohol per kilo of body weight, required to kill in from 24 to 48 hours.	Relative toxicity.
Methyl alcohol 7.2 to 9.02	0.8
Ethyl " " 6.25 " 7.44	1.
Propyl " " 3.0 " 3.46	2.
Butyl " " 2.1 " 2.44	3.
Amyl " " 1.7 " 1.95	4.

Joffroy and his pupils would express the *experimental toxic equivalent* of these alcohols, as found by slow intravenous injections in dogs whose blood had been rendered non-coagulable by the administration of leech extract, by the following figures:—

	Toxic equivalent for dogs.	Relative toxicity.
Methyl alcohol 16.95 c. c.	0.46
Ethyl " " 7.80 "	1.
Propyl " " 2.23 "	3.5
Butyl " " 0.97 "	8.0
Amyl " " 0.43 "	18.5

For chemically pure ethyl alcohol Joffroy and Servieux find the *true toxic equivalent* for dogs to be 8.65 c. c., that of the ethyl alcohol of commerce being 7.80 c. c.; for rabbits the equivalents for these two varieties of ethyl alcohol are 8.20 c. c. and

7.60 c. c. The ethyl alcohol used in the arts and the alcohols described as "*les alcools de mauvais gout de tête et de queue*" have nearly the same toxic equivalent as a good commercial sample of ethyl alcohol, the figures found varying but little from 7. Joffroy concludes that, as far as *acute* poisoning is concerned, the poorly rectified and bad tasting spirits are not so much more poisonous than the well-rectified varieties, as has usually been assumed.

The true toxic equivalent for methyl alcohol for the rabbit is put at 10.90 c. c., and for the dog it may be as low as 9.10 c. c. when the dose is so graded that death does not follow in less than sixty-five hours.

Picaud's results, which have already been cited, are more nearly in accord with these than with those of Baer; on the other hand, the earlier results of Dujardin, obtained by the method of subcutaneous injection in dogs and pigs, are more nearly in accord with those of Baer.

A large number of other investigators who have worked at this subject from different points of view all bear witness to the general statement of the greater toxicity of the higher alcohols for animal life in general. Among these may be named Pelletan, Fürst, Dalström, Cros, Huss, Rabuteau, Dogiel, Richardson, Stenberg, Laborde, Magnan, Otto, Strassmann, V. Mering and Schneegans, Gibbs and Reichert, Audigé, Daremberg, and Feré. These writers have not all interpreted their results in the same way. Some attach more importance to the higher alcohols from a hygienic point of view than others; some draw no deductions of a practical character, but are content with a mere statement of their results.

More important than the determination of the toxic equivalent of the several alcohols taken separately is the knowledge of how the addition of small amounts of the higher alcohols to ethyl alcohol influences its toxicity.

Rabuteau (1870) declares that the addition of fifty and even of twenty-five centigrams of amyl alcohol to a half litre of good wine caused a feeling of oppression instead of the agreeable state of mind which was always produced when the unpoisoned wine was taken. He also describes in vivid language the effects produced in his own person when he drank a half litre of ordi-

nary wine, purchased in one of the poorer wine shops of Paris. He felt as though a band were fastened about his temples, his mind was clouded; the intoxication experienced by him is described as "bizarre, stupid, brutish." From Rabuteau's account it can only be inferred that he drank a wine largely fortified with fusel oil or with alcohol of the lowest grade. It may be remarked in this connection that great improvements have been made in the preparation, not only of the alcohols of commerce, but of wines and other beverages, since Rabuteau's day. The experiments of Magnus Huss (1852) also show that amyl alcohol acts on human beings in the manner described by Rabuteau. In doses of one eighth to one half grain it caused no toxic symptoms; doses of one to two grains were followed by a sensation of oppression in the chest and a temporary feeling of dizziness; doses of three to four grains acted like a gastro-intestinal irritant, causing a burning sensation in the epigastrium, colic, vomiting, and diarrhœa. Given in small doses to persons who were suffering from the effects of the abuse of brandy, rum, etc., and who showed such symptoms as tremors, pain in the chest, paræsthesia, unrest, a sensation of general weakness, etc., it frequently had the effect of alleviating these symptoms. Huss concludes that it is not probable that any important part of the damage done to the nervous system of drunkards is to be ascribed to this alcohol and gives among other reasons for this opinion that the total quantity of amyl alcohol contained in twelve or fifteen glasses of brandy or whiskey amounts to only one or one half grains.

Whatever may be the rôle of small quantities of the higher alcohols in the way of assisting ethyl alcohol to produce the symptoms of *chronic* alcoholism, it seems well established that those beverages which contain more of these alcohols, such as the poorer grades of spirits and wines, more easily give rise to minor disturbances of the health, such as headache, mental depression, gastric irritation, etc. Richardson thought it probable "that the higher alcohols are the cause of that coldness, lassitude, and depression induced by the dinner with bad wine."

Joffroy and Servieux and other later experimenters all agree in stating that the untoward effects, as lassitude, want of appetite, and slow recovery, are more marked in animals that receive the poorer grades of spirits, even though the toxic equivalents

of these *alcools de mauvais gout* are but little lower than those of the purer spirits. The experiments on animals in this respect agree, therefore, with the experience of mankind.

Stenberg experimented on rabbits with mixtures of pure ethyl alcohol and pure amyl alcohol and found that the addition of four per cent. of amyl alcohol had but little influence on the intensity and duration of the symptoms of acute intoxication. Strassmann found that in the case of dogs the addition of amyl alcohol to the extent of three per cent. caused death to ensue in less than half the time as compared with alcohol containing none of the higher alcohol. The addition of one per cent. of amyl alcohol increased the severity of some of the symptoms of poisoning, but not sufficiently to hasten death to the slightest degree. G. Baer has lately taken up this point in careful experiments on dogs and rabbits and has expressed his results in the form of tables giving the toxic equivalent for rabbits of various mixtures of ethyl alcohol and the higher alcohols.

				Mild form of intoxication. Grams per kilo animal.
Pure ethyl alcohol	.	.	.	4.1
" " " and 1%	propyl alcohol	.	.	4.04
" " " " 1%	butyl "	3.92
" " " " 1%	amyl "	3.80
				Medium type of intoxication.
Pure ethyl alcohol	.	.	.	6.15
" " " and 1%	propyl alcohol	.	.	5.99
" " " " 1%	butyl "	5.83
" " " " 1%	amyl "	5.67
				Severe type of intoxication.
Pure ethyl alcohol	.	.	.	7.44
" " " and 1%	propyl alcohol	.	.	7.28
" " " " 1%	butyl "	7.04
" " " " 1%	amyl "	6.82
				Mild type of intoxication.
Pure ethyl alcohol	.	.	.	4.1
" " " and 2%	propyl alcohol	.	.	4.04
" " " " 2%	butyl "	3.80
" " " " 2%	amyl "	3.64
				Medium type of intoxication.
Pure ethyl alcohol	.	.	.	6.15
" " " and 2%	propyl alcohol	.	.	5.82
" " " " 2%	butyl "	5.59
" " " " 2%	amyl "	5.02

						Severe type of intoxication.
Pure ethyl alcohol	7.44
"	"	"	and 2%	propyl alcohol	.	7.02
"	"	"	" 2%	butyl	"	6.11
"	"	"	" 2%	amyl	"	5.85
						Mild form of intoxication.
Pure ethyl alcohol	4.1
"	"	"	and 4%	propyl alcohol	.	3.5
"	"	"	" 4%	butyl	"	3.16
"	"	"	" 4%	amyl	"	2.84
						Medium form of intoxication.
Pure ethyl alcohol	6.15
"	"	"	and 4%	propyl alcohol	.	5.09
"	"	"	" 4%	butyl	"	4.62
"	"	"	" 4%	amyl	"	3.89
						Severe form of intoxication.
Pure ethyl alcohol	7.44
"	"	"	and 4%	propyl alcohol	.	6.06
"	"	"	" 4%	butyl	"	5.50
"	"	"	" 4%	amyl	"	4.66

Baer's tables show that the addition to ethyl alcohol of one per cent. of the three next higher alcohols has but a minimum influence in increasing its toxicity for rabbits. The addition of one per cent. of the more poisonous amyl alcohol shows that only very little less ethyl alcohol is required to produce the various degrees of intoxication. The addition of two per cent. of one of the higher alcohols causes an appreciable increase in toxicity, and the addition of four per cent. of amyl alcohol a very considerable increase, so that a severe type of poisoning results, the toxic equivalent being 4.66 grams per kilo for the mixture, as against 7.44 grams for ethyl alcohol.

It would appear, then, that far larger quantities of the higher alcohols must be added to ethyl alcohol than are found in even the worst alcoholic beverages before we can attribute to these higher alcohols any great share in the fatal outcome of an acute poisoning with whiskey and the like.

It will now be in place to consider the action of the esters to which brandies, wines, etc., owe so large a part of their flavors. Albertoni and Lussana have studied the action of the ethyl esters of acetic, butyric, and cœnanthic acids on both animals and human beings. The results obtained by these authors point to the conclusion that compounds of this nature play no

rôle in acute intoxication by alcoholic beverages. More recently Krautweg and Vogel have published detailed pharmacological researches on the action of various esters. Krautweg demonstrated that the intravenous injection of 0.1 gram or the subcutaneous injection of 0.5 gram, of ethyl acetate acted on rabbits as a respiratory stimulant and caused a slight but temporary rise of the blood pressure. Krautweg considers this ester to be a more powerful stimulant than camphor.

Vogel studied a whole series of esters, with particular reference to their action on the respiration. His results show that small quantities of these esters stimulate the respiratory centres and cause an increase in the volume of air taken into the lungs in a given time; also that large quantities paralyze the respiratory centre and bring on convulsions. The only conclusion of practical importance that can be drawn from these experiments on animals is that certain alcoholic beverages, like wines of high flavor, are more stimulating to the respiration than preparations which contain only traces of these volatile constituents.

It should be borne in mind, however, that experiments on the air intake of so sensitive an animal as the rabbit are likely to lead to exaggerated opinions as to the power of these agents as respiratory and circulatory stimulants. Associated with much alcohol as they are in alcoholic beverages, their full action will hardly be developed to the same extent as when administered alone, any more than a little atropine given in combination with a great deal of morphine will develop its full power as a respiratory stimulant.

As far as they touch our present discussion, we may safely say that these esters play no rôle in acute intoxication; that is to say, they are not present in any such amount as to cause any part of the intoxication due to an excess of wine, brandy, etc.

French writers, as Magnan, Laborde, and others, have studied the action of absinthe, of essences, "wine oils," and "bouquets," which are used by compounders in the artificial preparation of cognacs, liqueurs, etc.

The liquor sold in France under the name of absinthe contains all the way from forty-seven to eighty per cent. of ethyl alcohol and is highly flavored with the aromatic constituents of wormwood, anise, fennel, coriander, *calamus aromaticus*, hysop, marjoram, etc., the proportion and selection of these flavors

varying with the special variety of the absinthe. As long ago as 1865 Lancereux maintained that alcohol is, from a quantitative point of view, the chief poison of absinthe. Yet there can be no doubt that if the alcohol were removed from absinthe, its excessive consumption would still wreck the nervous system, because of the presence in large amount of the aromatic constituents enumerated.

In weak doses absinthe induces in animals well-marked muscular tremors, or abrupt jerking movements, like those observed after stimulation by electricity. With larger doses epileptiform attacks and loss of consciousness are observed, and the animal falls over and stiffens in tonic convulsions which constitute the first stage of the fit. Unlike pure alcohol, which time requires for the production of delirium, this fluid gives rise to hallucinations from the very first. Between the epileptic attacks states of delirium are often observed, and delirium without epileptic seizures is also described.

In a word, the series of symptoms designated as absinthism, in human beings, can be produced in animals by the administration of the liquors in question.

The difference between it and acute alcoholism is to be ascribed to the volatile and aromatic constituents which accompany the alcohol.

The "wine oils" of the compounders are, of course, very poisonous taken as such, causing at first a marked excitement of the nervous system, shown in an increased respiratory rate and mental excitement, and death ensues later because of a central paralysis of the respiration. When the product which is prepared from such a "wine oil" is finally offered for sale, it may on examination be found to be no more fatal as a poison than the corresponding natural product. That is to say, its toxic equivalent may be the same as that of the natural product of the same name. This is not saying that the two preparations will have the same minor effects in equal doses, for the artificial product may possibly induce lassitude, headache, etc., while the natural product has no such effect.

A preparation known as *Essence de noyau* was found to contain benzaldehyde and benzonitril; other preparations contain cinnamic aldehyde and the methyl ester of cinnamic ester. As a rule, however, those preparations which are to serve as

the flavoring base of artificial wines, brandies, liqueurs, etc., contain only such esters, aldehydes, and higher alcohols as are found in natives wines and brandies.

It cannot be doubted that there is considerable ground for alarm concerning artificially prepared alcoholic products, and that legislation might well be directed to the question.

One other constituent of alcoholic beverages deserves brief consideration at this point, and that is furfurol, or pyromucic aldehyde. According to Roeques, one litre of rum contains only from 0.015 to 0.040 gram, one litre of cognac 0.005 to 0.015 gram, one litre of wine 0.003 to 0.006 gram of this aldehyde. It requires over 0.200 gram per kilo of body weight of this substance to kill a dog, somewhat less to kill a rabbit. While its toxic equivalent is high as compared with ethyl alcohol, it should be borne in mind that it would require about two grams to kill a small dog weighing ten pounds, or the quantity contained in seven or eight gallons of cognac.

Regarding all of the constituents of alcoholic beverages for the moment as poisons, their relative toxicity in cases of acute poisoning will best be understood if we put the results that have been discussed in the form of tables, as has been done by Antheaume. Analysis shows that a litre of rum, for example, contains on the average

500 c. c. of ethyl alcohol,	
0.763 " " ethers,	
0.153 " " aldehydes,	
0.384 " " higher alcohols,	
0.034 " " furfurol.	

The toxic equivalents of these constituents are as follows:—

Of ethyl alcohol	7.80 (Joffroy),
" ethers	4. (Dujardin-Beaumetz),
" aldehydes	1. (Joffroy),
" furfurol	0.14 (Joffroy),
" higher alcohols	1.50 (Dujardin-Beaumetz).

Assuming now that the toxicity of a given beverage is equal to the sum of the toxicities of its several constituents, we find that

500 c. c. of ethyl alcohol will kill 64.102 kilograms.					
0.763	"	"	ethers	"	0.191
0.153	"	"	aldehydes	"	0.153
0.034	"	"	furfural	"	0.243
0.387	"	"	higher alcohols	"	0.258
Total				64.947	"

A glance at the table shows that the alcohol of this litre of rum will alone destroy 64.102 kilograms of animal life, be it dog or man. The by-products are therefore of only secondary importance as toxic agents. Similar tables could be drawn up for cognacs, whiskey, wines, etc., and in every instance it would be found that ethyl alcohol is the preponderatingly harmful ingredient. Absinthe and liqueurs are exceptions, as already stated, in that harmful, non-alcoholic products are here present in larger proportions. Data in the form of the toxic equivalents of all of the constituents of these liqueurs are not at hand, but it may safely be asserted that here also a large share of the toxicity is to be ascribed to the seventy-five per cent. of alcohol which they contain.

4. INFLUENCE OF THE CONSTITUENTS OF ALCOHOLIC BEVERAGES IN CHRONIC ALCOHOLISM.

We may now take up the very important question as to how far the higher alcohols and other by-products of an intoxicating nature are responsible for the symptoms of *chronic* alcoholism. It is, after all, this form of alcoholism with which the hygienist and pathologist is most concerned.

A very important point comes up for consideration in this connection. Experiments have shown that the relation which exists between the various alcohols, esters, etc., as established by the tests for acute intoxication, does not always obtain when these substances are studied in experiments which extend over a long period of time. A substance like methyl alcohol, which is less toxic than ethyl alcohol in a single experiment with lethal doses, may prove to be the more poisonous of the two when both are administered in small quantities during a long period of time. Pohl, Joffroy, and others have found that methyl alcohol, administered to animals over long periods, causes serious nervous symptoms and produces pathological lesions in doses in which ethyl alcohol has little effect. Pohl found that he

could feed dogs for many months, almost a year in fact, with small quantities of either ethyl, isobutyl, or amyl alcohol, without noticeable injury. Thus, a young dog weighing 1190 grams at the beginning of the experiment received a total quantity of 752 c. c. of amyl alcohol in the course of 220 days. In spite of repeated drunkenness the animal gained in stature and also increased in weight to 4700 grams during the period. At first one cubic centimetre of the amyl alcohol sufficed to cause profound intoxication, but later on this result could only be obtained with five cubic centimetres. When, however, Pohl administered methyl alcohol in quantities of from 15 to 20 c. c. to dogs, at intervals of two days, the animals never lived more than a few weeks, and the intoxication was always of a more severe type than after ethyl alcohol. After being made drunk with ethyl alcohol the dogs awoke from their stupor apparently normal. After methyl alcohol in equivalent quantities the drunken sleep continued into the following day and even longer, the animals refused to eat, were dull and spiritless, and only recovered their usual appetite and spirits after three or four days. Rabbits tolerated methyl alcohol even less well than dogs. The single, constantly occurring pathological change discovered by Pohl, in animals slowly poisoned with methyl alcohol, was a marked fatty degeneration of the liver. The amount of fat that could be extracted from the liver of a healthy dog was found to be 16.6 per cent. of the dry weight of the liver, while from the livers of dogs poisoned with methyl alcohol 37.5 per cent. and 37.9 per cent. was extracted.

Joffroy and Servieux also report that methyl alcohol causes the death of dogs in a few months, when it is given in daily doses of from 2 to 3 c. c. for each kilogram of body weight.

The reason that this alcohol is so poorly tolerated when administered for a long period is to be found in the fact that a considerable proportion of it is turned into formic acid in its passage through the body. Pohl maintains that the excretion of formic acid in the urine reaches its maximum on the third, or even as late as the fourth, day after a single administration of methyl alcohol, and that this protracted excretion is not due to the retention of the acid in the body, but rather to a delayed acid conversion in the tissues of the methyl alcohol itself, or of some transformation product of it. According to Bongers, the

urine of the second day contains the largest amount of the formic acid, and the excretion continues into the third day. The urine of the first and second day also contains considerable quantities of unchanged methyl alcohol.

The formic acid thus produced in the body is a powerful irritant and constitutes a menace for many important organs.

In this connection it may be remarked that ethyl alcohol is also less easily and quickly oxidized than has been supposed. It is well known that when moderate quantities of this alcohol are consumed only a very small amount is eliminated as such and escapes oxidation. According to Gréhan (1896), who has made hourly examinations of the blood after the slow intravenous injection of an amount of properly diluted alcohol equal to one twenty-fifth of the weight of the blood, twenty-four hours elapse before the alcohol entirely disappears from the blood. One hour after the completion of the injection the volatile oxidizable products which can be distilled from the blood, expressed in terms of alcohol, equal 0.72 c. c. of absolute alcohol; even eighteen hours after the injection the oxidizable distillate still contains the equivalent of 0.15 c. c. of absolute alcohol, while after the lapse of twenty-three hours and twenty minutes no oxidizable distillate is obtained from the blood. To this discovery of Gréhan's we must add the more recent observations of Thomas, who has shown that the blood of rabbits intoxicated with ethyl alcohol contains more volatile fatty acid, probably acetic, than is normally present, and that its alkalinity is much reduced and its carbonic acid content diminished. Whatever may be the practical significance of these intermediate products of oxidation thus shown to exist in the body fluids, their existence is of scientific interest and compels further study of this question.

Although methyl alcohol is more dangerous to the economy than ethyl alcohol when its consumption extends over a period of time, but little influence can be attributed to it in causing the symptoms observed in chronic alcoholism. For, as has already been stated, this alcohol is rarely present in adulterated alcoholic beverages, and then only in very minute amounts. As an agent in chronic alcoholism it is of no importance.

Furfural, which as already stated is found in very small quantities in alcoholic beverages, can likewise be thrown out of

consideration as playing a rôle of importance in the symptomatology of chronic alcoholism. Riche has found that a litre of rum contains only 0.015 to 0.040 gram and a litre of cognac or armagnac only 0.005 to 0.015 gram of this substance.

Joffroy has found the toxic equivalent of this substance to be only 0.14 for rabbits and 0.20 for dogs, as against 8.20 to 8.60, the true toxic equivalent of ethyl alcohol for these animals. Assuming that man is as sensitive as the rabbit for furfural, it would require the consumption of ten grams at one time on the part of a man weighing seventy kilograms in order that death should result. This substance is therefore a fairly powerful poison, but it would require from three hundred to seven hundred litres of rum or brandy to furnish the fatal dose. When it is further taken into consideration that the animal organism establishes a tolerance for this substance, it will appear evident why no importance attaches to this by-product.

On the 17th of March, 1897, Joffroy gave a demonstration in Paris, in which he showed a dog which had been receiving furfural since March 1st of the preceding year. At the time of the demonstration the health of the animal was satisfactory, and this in spite of the fact that at this time it was receiving each day a dose of furfural which was stated to be more than half as large as the fatal quantity when administered by the method of intra-muscular injection to an animal not habituated to its use. This substance, therefore, behaves very differently from methyl alcohol, being oxidized or otherwise disposed of with less damage to the organism.

The two examples that have been cited show how necessary it is to study the behavior of *each* of the by-products in alcoholic drinks when administered by itself over a long period before we can attribute to each its own share of the harmfulness which ensues upon the prolonged and excessive use of spirits, wines, etc. It is not enough to know the toxic equivalent of an alcohol or of a by-product as measured by the experiments detailed in the preceding section in order to determine precisely what effects will follow their prolonged administration. But experiments on animals involving the daily and prolonged administration of small quantities of *each* of the several higher alcohols which are found to exist in traces in distilled liquors are not as numerous as could be desired.

Reference has already been made to the work of Pohl (1892), whose dogs were fed for many months, at intervals of one or more days, with small quantities of isobutyl or amyl alcohol, without noticeable injury.

Long before Pohl, however, Dujardin and Audigé had learned that the pig, for example, will tolerate fusel oil for a long time. These experimenters found that two pigs which had received with their food, at short intervals during three years, certain quantities of a distillation residue containing much fusel oil died at the expiration of the time, while other pigs that had been similarly fed with ethyl alcohol remained alive.

Joffroy and Servieux in recent years also testify to the more deadly action of amyl alcohol when administered over a long period of time, as compared with ethyl alcohol.

The esters, to which wines owe their bouquet and which are also present to a small extent in brandies and other spirits, may safely be asserted to play no rôle of importance in the symptomatology of chronic alcoholism. They are very volatile substances, hardly more poisonous than ordinary ether, and their amount in wines of high flavor probably never exceeds a small fraction of one per cent.

It now remains for us to discuss the action of pure ethyl alcohol when administered to animals over a long period of time. As we have repeatedly said, this is, from a quantitative point of view, the chief alcohol in all forms of alcoholic drinks, being present in amounts varying from two and a half per cent. in the *Einfach Bier* of the German to seventy-five per cent. in absinthe. We have shown that it is less toxic than the higher alcohols when its action is measured by the standards of "acute toxicity," and we shall now show that this is true also for experiments that extend over a long period. Ethyl alcohol alone, then, is poisonous enough to account for all the evils of intemperance. It is in reality needless to consider the small quantities of higher alcohols, aldehydes, etc., that are associated with it in alcoholic beverages. Exception must, of course, be made when absinthe and a few similar preparations are considered, in which volatile flavoring principles, so potent in their action on the nervous system and other organs, are present in considerable number and quantity.

In 1896 Joffroy and Servieux began a series of experiments

in which they studied the effect on dogs of daily intoxication with ethyl alcohol and other constituents of alcoholic beverages. It required the free administration of diluted alcohol for a period of eight months to produce noticeable pathological lesions of the digestive tract and kidneys of one of them, while a second, a young and vigorous dog, seemed to have sustained no apparent injury at the end of the period; it was even thought by the authors that this animal would long resist the poisonous action of the alcohol. The first of the group refused, after a time, to lend himself to the experiments, and the second succumbed, after forty-six days, to an epileptiform attack which came on while the animal was in heat.

These authors, like many others, noted how greatly animals vary in their resisting power to this agent. Ability to consume food freely during the alcohol periods appears to be an important factor in delaying the appearance of pathological lesions. Combemale, for example, describes a very greedy dog, who daily consumed double rations of food during a six months' period of alcoholization and who would still make efforts to eat when he was too much intoxicated to walk. This animal presented no typical signs of chronic alcoholism after this long indulgence. Like others, Combemale notes that animals who do not feed well rapidly develop symptoms of disease.

The influence of age is well illustrated in the experiments of Koller, which were made upon young dogs. After any but very small doses a marked change is produced; loss of appetite is soon followed by symptoms of nervous instability, convulsions, and tetanic paroxysms. Faulty nutrition is shown in the roughness of the hair, generally under-nourished appearance, and arrested growth. Irritation of the digestive tract from the employment of strong solutions of alcohol, say thirty-three per cent., is soon followed by a deficiency of food absorption, and this in turn must cause what Edinger has called a condition of *stress* in the nerve cells, or, in other words, an increased predisposition to the harmful action of the alcohol.

It is not the purpose of the present paper to describe in detail the pathological lesions that have been met by various investigators in the course of their experiments on animals subjected to the action of alcohol or alcoholic beverages. This difficult task will be dealt with by specialists in the field of pathology.

On consulting the literature of the subject, the reader will find that the experimental pathologist finds great difficulty in reproducing in animals the exact clinical and pathological conditions found in man. The gastro-intestinal and nervous disturbances are more nearly comparable to the corresponding occurrences in man than are the lesions of the nerves, nerve cells, liver, kidney, heart, etc., to the morbid changes in man. Typical cirrhosis of the liver, for example, which is also not of the most frequent occurrence in the human pathology of alcohol, has not been seen in these experiments. Strauss and Blocq and v. Kahlden, however, note very decided lesions of the liver in their animals, and the latter author also attributes to alcohol a not unimportant rôle in the etiology of nephritis. Those who, like Thomas, have failed to find any lesions of the liver, kidneys, or arteries in rabbits, even when these animals have been kept in a state of daily intoxication for several months, have underestimated the influence of age, nutrition, time, and other circumstances in the production of a predisposition to the effects of alcohol.

The experiments with pure ethyl alcohol of the authors already cited, as well as those of Strauss and Blocq, Kremiansky, Afanassiejew, Spaink, Carrara, v. Kahlden, Hodge, and others, on special phases of the pathological problem, in spite of contradictions and differences of opinion and the limitation just referred to, nevertheless force upon one the conviction that the excessive use of alcoholics actually causes in man those anatomical lesions which students of medicine have long ascribed to them.

When all the facts at hand are summed up, we must concur in the opinion long ago expressed by Magnus Huss (1859), and in late years by Joffroy and others, that the impurities and by-products of alcoholic beverages may be neglected altogether as a cause of the drink evil. No matter how high the toxic equivalent of these by-products may be, they are present in such minute quantities in all alcoholic drinks that their rôle in causing the lesions of chronic alcoholism is one only of secondary importance.

As Antheaume has well said, the drink evil is nothing but the abuse of ethyl alcohol.

In 1884 the Swiss physician, Steiger, stated it as his opinion

that the harmfulness of excessive brandy drinking could not be attributed to the fusel oil which it contained, but rather to its ethyl alcohol, for the reason that the inhabitants of the Jura, among whom intemperance with all its attendant evils is very prevalent, drink only a highly purified brandy containing no fusel oil.

But we cannot say that all these experiments, conclusive as they are as to the toxic action of pure ethyl alcohol, contradict the impression of experienced judges that a "sound" alcoholic beverage is less productive of minor ill effects, such as indigestion, lassitude, and headache. It is quite possible that these minor effects will in the future be found to be of greater pathological significance than is now believed.

Improvement in the quality of all alcoholic beverages, in the sense now well understood by experts in that field, is certainly as desirable as raising the standard of purity in regard to all articles consumed by us. A cautious man will avoid salicylic acid in his beer or his canned vegetables, even though the pathologist fails to show that a six months' use of it injures the kidneys. Legislation to this end might be beneficial on broad hygienic grounds, although of itself alone of little effect in decreasing the larger evils of intemperance.

It has been the aim of the Swiss government to improve the quality of the brandy consumed by its people, and at the same time to check its excessive use, by substituting for it wine and beer, this substitution being assisted by the abolition of certain duties on these latter. Milliet says, "The struggle with alcohol did not rest with these achievements, the increased price of distilled liquors, the cheapening of wine and beer. These general measures were accompanied by two special ones whose importance is by no means insignificant, the regulation of distilleries and the application of one tenth of the monopoly receipts to the struggle with alcoholism."

According to Ladame, the combined action of these measures has caused a reduction of twenty-five per cent. in the consumption of brandy by the Swiss people. To what extent this reduction represents an improvement in the health of the people, or lessening of injury to vital organs, cannot be determined from such a statistical statement. The more concentrated alcoholic beverages are the more harmful ones, as has already been

stated, but wines and beer, taken in excess, must also develop the poisonous action of the alcohol contained in them. Legislation directed toward the drink evil will always have to take account of the facts established by studies like those outlined in this paper, that the "best" alcoholic beverages are as capable of producing this evil as are the poorest. Purification of these beverages alone cannot hope to eradicate it.

II. ACTION OF ALCOHOL ON THE VASCULAR MECHANISM.

It has been well said that "when a substance acts on as many different organs as does alcohol, it becomes no easy matter to get at its immediate specific action on any one organ."

Any inquiry into the nature of its action on the several parts of the vascular apparatus, as on the heart or vessels or their controlling nerve centres, must be conducted under several heads. We must inquire into the direct action of the agent on each of these parts of the vascular apparatus taken by itself and must then conclude what is its action on the entire apparatus when each part is in vital connection with the rest. It has already been stated that the cerebral effects of moderate quantities of alcohol have certain physiological accompaniments, such as a flushing of the face, or a greater fullness, softness, and rapidity of the pulse. These and other evidences of "stimulation" are so frequently observed that the medical profession has long spoken of alcohol as "heart stimulant."

Now it is well known that under the influences of a drug changes in the pulse may take place which are not the consequence of a *direct* action of that drug either on the heart, the walls of the blood vessels, or the nervous centres controlling the action of the heart and the calibre of the vessels, but which are the consequences of an indirect action, exerted on mucous surfaces, or of a cerebral action, which induces the individual to make movements of the body, which in turn affect the rate and character of the pulse.

We shall see that numerous investigators have shown that when alcohol is administered in moderate doses and well diluted, so that local irritation in the mouth and stomach is avoided, and when precautions against muscular movements are taken, no changes in the pulse rate occur.

1. RESEARCHES ON THE INFLUENCE OF ALCOHOL ON THE PULSE RATE.

One of the best of the earlier researches in this field was published by Zimmerberg in 1869. This author has not always met with the appreciation to which his work entitles him. It would seem that not one of the four American writers who have discussed his experiments could have read them in the original, for they assert either that his results on animals are valueless because only large or toxic doses are used or that he did not experiment at all on man. Neither of these statements is correct. Zimmerberg was also one of the first to point out that certain animals, like the rabbit, are not well adapted for experiments with a drug like alcohol when no anæsthetic is employed. The excitement induced in them by handling them, by the introduction of a tube into the stomach, etc., is so great and introduces such disturbing factors into the experiment that the conclusions drawn from it are often worthless.

To illustrate the uselessness of this animal for experiments with alcohol, Zimmerberg introduced 20 c. c. of distilled water, by means of a sound, into the stomach of a rabbit which a few days before had been employed in a similar experiment in which alcohol was used. The protocol of the experiment is so very similar to those noted down in many experiments on alcohol that I have thought it worth while to give it in its entirety: —

(Rabbit of average size, not tied down.)			
Time.	Respirations in 15 seconds.	Pulse in 10 seconds.	
12.34	13	33.	
12.39	19	34.35	Slight excitement.
12.43	11	32.	
12.47	10	30.33	
12.57	14	30.32	
12.58	11	28.	Animal quiet.
1.09	Injection of 20 c. c. distilled water into the stomach.		
1.10	14	46.45	
1.13	12	53.	} The heart action more plainly to be felt ; the heart sounds louder.
1.15	12	49.47	
1.18	10	43.46	
1.22	11	40.41	
1.27	11	36.39	
1.32	11	38.40	
1.38	10	40.	
1.44	9	41.	
1.49	10	43.38	
1.55	10	34.36	
2.0	10	32.34	

How very markedly the pulse rate was influenced by the mere injection of a little water into the stomach is shown by a glance at the above table. Had Zimmerberg taken a blood pressure tracing he would, no doubt, have obtained first a rise and then a fall of pressure. The above changes in the pulse are brought about in a reflex manner. During all this time it may be assumed that the animal was quiet; for in all his experiments Zimmerberg was careful to make a note of every movement of the animal. All experimenters will share Zimmerberg's opinion as to the unfitness of the rabbits for experiments in which the use of an anæsthetic is unallowable.

Even Wilmanns, a writer who will be referred to later and who has used the rabbit to show that alcohol is a respiratory "stimulant," makes the following admission: "During the past winter, I had at my disposal a litter of rabbits, with which no experiments whatever could be made; the slightest noise, or the injection of the alcohol, made them extremely restless (*äusserst unruhig*), and naturally caused the respirations to be much accelerated."

In view of these facts we shall pay no attention to such experiments as those of Tscheschichin, who injected 15 c. c. of dilute alcohol into the stomach of a rabbit and found that in the course of twenty minutes the pulse increased from 120 to such an enormous rate that it could not be counted. Then, too, experiments like those of Ruge on dogs, in which the pulse rate rose to 250 and more when the animals were rapidly anæsthetized by alcohol, must be thrown out of consideration here, as they merely illustrate a phase of the toxic action of alcohol.

Zimmerberg's experiments on frogs, cats, dogs, and men led him to conclude that alcohol caused no increase in the pulse rate, either in the case of the unfettered animals, or in man, when the *proper precautions were taken against local irritation and movements of the body*. The following protocol, in which not too large a quantity of alcohol was administered, that is, not too large, considering that it was introduced into the stomach and not directly into the circulation, may be given as an illustration of his experiments on animals: —

(Dog, poodle bitch of average size, 2 years old, placed on her side on a table, not fettered.)

Time.	Respirations in 15 seconds.	Pulse in 10 seconds.	
12.15	6	20	Animal quiet.
12.25	7	18	
12.30	—	20	
12.35	5	24	Slight excitement.
12.50	Injection of 10 c. c. alcohol of 30 per cent.		
12.51	6.5	22	
12.54	6	23	
12.58	5.5	21	
1.02	5	19	
1.06	6	17	
1.09	6	19	
1.12	6	18	
1.16	7	25	After walking a few steps.
1.20	6	20	
1.20	7	22	

In the experiments on men various precautions were taken; the individuals were put to bed, alcohol of forty-four per cent. was administered sweetened with sugar, and in one case cochineal and tincture of quassia were added, so that the individual believed he was taking a medicine. All of the six individuals experimented on were accustomed to the use of alcohol; their ages varied from nineteen to fifty-eight years. The quantities of alcohol administered varied from three to six ounces of a solution which contained forty-four per cent. of alcohol. In no instance was the pulse rate influenced.

The results of the experiments of Cuny Bouvier (1869) agree with those of Zimmerberg. Bouvier's object was the study of the influence of alcohol on the body temperature. He gives countings of the pulse rate in experiments on Dr. Kemmerich and on a second individual, both of whom were accustomed to the use of alcoholic beverages. Neither small nor large doses of pure ethyl alcohol, cognac, whiskey, or wine had any effect on the pulse rate of these two individuals. Dr. Kemmerich lay in bed, lightly covered, during the experiments.

Marvaud (1872) describes a number of experiments on the pulse rate of four young men. The sphygmograph of Marey was used, and the pulse tracings are described in Marvaud's treatise on the *Physiological Action of Alcohol*.

In Experiment 1 a man twenty-three years old, in good health and fasting, had a pulse rate of sixty-eight; ten minutes after

taking thirty grams of brandy his pulse had risen to seventy-two.

The second man was twenty-three years old, also in good health, pulse sixty; five minutes after taking thirty grams of brandy the pulse was sixty-four, and fifteen minutes after the administration it was sixty-eight.

In Experiment 3 a young man of twenty had a normal pulse rate of sixty-eight. Five minutes after taking fifty grams of brandy his pulse rate was seventy-two, and ten minutes later it was sixty-eight. In Experiment 4 no change in the pulse rate was observed, it being sixty-eight both before and after brandy.

The subjects of Experiments 1 and 2 were young men of very nervous temperaments, who stated that they were easily excited by spirits and coffee. It will be seen that the increase in the pulse rate in Marvaud's cases is not great, and it is probable that the observance of all the necessary precautions would have given a different result. Marvaud wrongly interprets his pulse curves to mean that alcohol lowers the arterial tension. He concludes that alcohol, so far from being an excitant for the heart, really moderates and weakens its contractions, and that it is only at the beginning of the administration, and under the influence of very small doses, that the heart shows a greater energy and frequency in its contractions.

Other observers have also repeated Zimmerberg's work, using smaller quantities of alcohol, and have reached the same conclusion, — that moderate quantities of alcohol well diluted with water have no influence on the pulse rate of healthy individuals. Thus Martin and Stevens (1883) give in the following table the results of this experiment on a young man of twenty-six, who had never, so far as he knew, drunk anything containing alcohol: —

Hour. P. M.	Pulse rate per minute.	Notes.
9.05	74	Subject lay down on bed at 9 P. M.
9.15	75	
9.25	71.5	
9.27	73	Drowsy.
9.30	72.5	
9.42	67.5	
9.50	69	

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Hour. P. M.	Pulse rate per minute.	Notes.
9.58	68	
10.08	—	Aroused.
10.10	73	(45 c. c. of water and sugar administered immediately before.)
10.15	72	
10.25	71	
10.30	70	
10.31	—	15 c. c. of alcohol in 15 c. c. of water.
10.35	71	
10.40	70	
10.45	72	Complains of slight dizziness.
10.52	70	
11.00	67	
11.07	69	
11.19	68	
11.25	67	
11.35	68	
11.48	70	
12.00	68	
A. M.		
12.10	69	

Jaquet and Von der Mühl¹ experimented on eight strong young men, all having sound hearts. The individuals were not aware of the nature of the experiments made on them, and psychical influences were, as far as possible, eliminated. The alcohol was administered in the form of a draught containing from 30 to 100 c. c. of a twenty per cent. solution of alcohol, with syrup of orange peel or tincture of quassia added. The subjects believed they were taking a medicine. The blood pressure on the temporal artery was taken by V. Basch's sphygmomanometer, and careful measurements of the pulse curves were made. The following table gives such of the results of these investigations as we wish to call attention to here:—

Individual.	Alcohol of 20% in c. c.	Pulse per min.		Blood pressure in mm. mercury.		Remarks.
		Before alcohol.	After alcohol.	Before.	After.	
I.	40	46	50 51	79	67 70	Perfectly quiet.
II.	30	86	88 85	—	—	Some feeling of heat, quiet, feels comfortable.
III.	50	56	60 60	86	92	Perfectly quiet.

¹ *Correspbl. Schw. Aertze*, 1891, xxi. 457.

Individual.	Alcohol of 20% in c. c.	Pulse per min.		Blood pressure in mm. mercury.		Remarks.
		Before alcohol.	After alcohol.	Before.	After.	
IV.	40	96	94	-	-	Comfortable.
			100			
V.	60	85	84	87	80	Quiet, comfortable.
			88		88	
VI.	60	62	62	81	84	Quiet, comfortable.
			62		85	
VII.	40	55	59	-	-	More talkative than usual; laughs without cause.
			66			
VIII.	100	56	69			
			71	-	-	Feeling of heat ; some excitement; and later vomiting.

An examination of the table of Jaquet and Von der Mühl shows how inconsiderable are the changes in pulse rate and blood pressure which small quantities of alcohol are able to produce. It is customary to attach but little importance to blood pressure results which have been obtained by V. Basch's sphygmomanometer; nevertheless, the instrument would have indicated any marked change in the blood pressure had such occurred in the experiments just cited.

Results directly opposed to those of Jaquet and Von der Mühl have been obtained by Weissenfeld in his study of the action of alcohol on the respiration. This author incidentally made a few blood pressure experiments with V. Basch's instrument on his own person. He took a heavy Greek wine in the morning, after having had only bread and butter and tea for his supper the night before. The following table gives the results obtained with 75 c. c. of heavy wine : —

Time. A. M.	Blood pressure in mm. mercury.
7.30	140
8.25 Took 75 c. c. Xeres wine, containing 18 per cent. alcohol.	
8.40	190
8.58	190
9.25	170

When the wine was taken some time after the usual breakfast the effect was less marked, the maximum pressure being 170 mm., and when equivalent amounts of diluted ethyl alcohol were taken the effect was still less, as shown in the following table :

Time, A. M.	Blood pressure.
9.	139
9. to 9.15, alcohol taken.	
9.15	145
9.40	160
10.20	150
10.50	150

The pulse rate in these experiments did not vary in a regular manner. In the first experiment it showed no variations of any importance; in the second it rose from seventy-two to eighty-four, and in the third it fell to sixty-four.

It is well known that long practice with the sphygmomanometer is a necessary condition for even fairly trustworthy results, and that this instrument cannot as yet compete with the mercurial manometer. This question, viz., the action of alcohol on the arterial pressure, will be discussed at greater length in a subsequent section.

The experiments thus far cited have given no evidence that alcohol in moderate quantities influences the pulse rate of healthy men when all disturbing and secondary influences are avoided. This statement would appear to hold both for those accustomed to its use in moderation and also for abstainers. The evidence just given in support of this statement could be further strengthened by pulse countings taken from blood pressure curves, and by data which are to be found in the protocols of writers who have studied some other aspect of the alcohol question but have incidentally given pulse countings. That the contrary opinion was ever held is due to the fact that no precautions were taken to eliminate the influences of local irritation or bodily movements.

The opposite position to the influence of alcohol on the pulse rate from that held by Zimmerberg, Martin, Jaquet, and Von der Mühl was taken by Parkes, E. Smith, Lichtenfels, Fröhlich, Duchek, and others.

Lichtenfels and Fröhlich, in 1852, published a monograph on the conditions which affect the pulse rate, which was of great importance in its day. These investigators maintained that wine and beer lower the pulse rate slightly during the first ten or fifteen minutes after their administration and then gradually increase it. Their results are vitiated by the following facts: they experimented on themselves; they did not

count the pulse for a long enough period before giving the alcohol; they laid too much stress on the minor and normal variations of the pulse; and lastly, they counted the pulse during fifteen seconds only, and then calculated averages for the whole minute from the quarter minute counts. In this way a serious error was introduced, for the respiratory rhythm so influences the pulse rate that in the first quarter of a given minute twenty beats of the pulse may be counted; while in the third or fourth quarter twenty-one or twenty-two beats may be observed. On multiplying the results by four we may, as Zimmerberg has pointed out, obtain results which differ by four or even eight beats, according as one or another quarter minute was used as the base of the calculation.

For the reasons given, the results of Lichtenfels and Fröhlich are of no value in relation to the point under discussion.

The observations of Duchek, made in 1853, are also of no value. This observer injected one and one half ounces of ninety per cent. alcohol into the rectum of a dog and observed a temporary increase in the pulse rate, which was, of course, due solely to reflex acceleration following on the great irritation set up by the alcohol.

In the writings of E. Smith (1859), on the effects of alcohol on the respiration of man, reference is incidentally made in the following words to its action on the pulse rate: "The rate of respiration was in almost all instances lessened in both of us, whilst that of pulsation was as constantly increased in myself, but not in Mr. Moul."

As the object of Smith's study was not to find the influence of alcohol on the pulse rate, all necessary precautions were not taken, and his statements on this point have no weight.

The extensive experiments of Parkes (1870-74), and of Parkes and Wollowicz on the influence of alcohol on the circulation, have also brought confusion into this question, chiefly owing to the fact that they did not sufficiently take into account the influences of local irritation and of variations in the dose.

In their first experiments Parkes and Wollowicz tested the influences of diluted alcohol and of brandy on a soldier twenty-eight years old, weighing 136 pounds, in good health, and accustomed to the daily consumption of one or two pints of beer. To this man the experimenters gave from one to eight ounces

of absolute alcohol a day, and they describe the effect as follows: "The effect on the circulation in the small vessels of the skin was very marked. The face, ears, and neck were flushed, and on the days of the large doses the face was slightly swollen. The skin of the trunk, as well as of the face, appeared hot to the man himself, and this was, no doubt, dependent on the same cause. It was some time before the turgescence of the cutaneous vessels lessened. Accompanying it was a sense of fullness and heaviness in the head," etc.

The pulse was counted every two hours with the man in the recumbent position. The highest mean pulse on any day before giving alcohol was 77.5 beats; the mean pulse of the first alcohol day (one fluid ounce of absolute alcohol) was 80; with two ounces, 78.3; with four ounces, 86; with six ounces, 98.3, but on this day there was fever; with eight ounces, 93.6; and on the last day with eight ounces, 94.7.

Similar results were obtained with brandy. The pulse tracings were submitted to Professor Burdon-Sanderson and were described by this physiologist as being of the *pulsus celer* type and as affording "no reason for supposing that the arterial pressure was increased."

These experiments illustrate only what happens under ordinary circumstances when an individual with an excitable vascular apparatus takes considerable strong alcohol or undiluted brandy and is not subjected to the experimental restrictions already cited. Neither the alcohol nor brandy was sufficiently diluted; the amounts given were far too large, and psychological, or subjective, influences were not sufficiently eliminated. These experiments fully corroborate what may be observed in daily life, but throw no light on the power of alcohol, introduced into the blood in moderate amounts, *without local irritation*, to affect the pulse rate.

In later experiments (1874) Parkes again tested the influence of brandy on the pulse rate, temperature, etc., of a young soldier. In this case "the pulse was taken on an average twenty-three times daily, from six in the morning until ten at night, the man being always in the recumbent position, until two o'clock every day."

The following are the averages for several days:—

Days.	Amount of undiluted brandy containing 50% of absolute alcohol.	Average pulse before brandy.	Average pulse after brandy.
1	1 fl. oz. at 11 A. M.	76.3	75.4
2	2 " " " "	79.9	73.3
3	4 " " " "	77.	77.2

The results of the fourth, fifth, and sixth days need not be given, as so much brandy was taken on some of these days that the appetite was destroyed and great depression, sickness, and headache resulted.

It will be noticed that the brandy caused no rise, but rather a depression of the mean pulse of the whole day. The mean pulse of the three hours immediately after the brandy was, however, increased on some of the days, as will be seen from the following table: —

Days.	Mean of the hours from 11 to 2 o'clock.	
	No brandy.	Brandy.
1	67.	69.
2	71.6	67.7
3	66.9	79.8

On the two days when a relatively smaller quantity of brandy (one to two ounces) was taken, the mean pulse in the three hours following its administration showed no change in rate worth mentioning, being a little above the normal mean on the first and a little below on the second day. The variations are undoubtedly not due to the alcohol. The third day may be thrown out, as it illustrates, if anything, only the toxic property of large doses.

The experiments of Parkes, when they deal with moderate quantities of alcoholic beverages, rather confirm than conflict with the careful experiments cited in the early part of this chapter. An examination of the tables of Parkes and Wolowicz, in which the results of the administration of claret are stated, also shows that the administration of more moderate quantities of wine, say ten ounces, had only a small effect on the pulse rate of healthy individuals.

The experiments of Wendelstadt, who has recently studied the effect of alcohol and of sherry on the respiration of man, may also be cited. These experiments were made in the laboratory of Professor Binz, of Bonn, the most noted among those who maintain that alcohol is a direct stimulant, and the observations made by Wendelstadt are the more interesting on this

account. Wendelstadt says, "The changes in the pulse rate were so inconstant that no conclusion can be arrived at in this particular. We nevertheless often noted an increase in the pulse rate, as in the individual No. VII." Now the pulse rate was not the especial object of study in these experiments. An examination of the protocols shows conclusively that, in the great majority of instances, after alcohol it showed variations too small to be considered.

Pulse countings are also given by still other investigators, both earlier and later, who have made the action of alcohol on body temperature, on the blood pressure, or on some other function, the real object of their study, but who nevertheless incidentally expressed an opinion on the point now under discussion. Some of these results, like those given in one of Bouvier's papers (1869), merely illustrate the reflex power of considerable quantities of strong alcohol (forty-four per cent.). Others, like those given by Dogiel, Castillo, Eagleton, and Cerna, will presently be discussed in the section of this paper devoted to the influence of alcohol on blood pressure, where it will be made evident that these authors draw unallowable inferences from their experiments.

The records of clinical medicine are of great interest in reference to the point under discussion. There can be no doubt that alcohol often acts as, and serves the purposes of, a "circulatory stimulant" in certain clinical conditions, such as shock or hemorrhage. In these conditions the weak pulse becomes fuller and stronger, the feeble heart beating more vigorously under the influence of the alcohol. Again, alcohol may act as a vascular sedative, a quick pulse being made slower as the rapidly beating, fluttering heart is induced to slow down to a regular rhythm. It is not in place here to discuss the manner in which these opposite clinical results are brought about by alcohol.

In the days when febrile diseases were treated with very large quantities of alcohol, a great reduction in pulse rate and in the rate of the respiration was a matter of daily observation. Without entering fully into the clinical literature dealing with the influence of alcohol on the pulse of the sick, I may refer briefly to the therapeutic studies of v. Jaksch. This writer tested the action of small quantities of alcohol, wine, and

brandy on the pulse rate and respiration of a number of children afflicted with rickets, bronchial troubles, tuberculosis, etc. Out of twelve children treated with small quantities of wine, the pulse was slowed in eight, hastened in two, and was entirely unaffected in two. Under the influence of eight cubic centimetres of brandy there was a decrease in the pulse rate in nine cases, an increase in one case, and no change in two instances. After 3.2 grams of pure ethyl alcohol properly diluted, the results were like those reported after brandy.

Instances enough could be cited from the records of medicine which go to show that alcohol acts on the pulse of convalescents and non-febrile patients, when the precautions taken by Martin and Stevens, Zimmerberg, and others are observed, in the same manner that it acts on the pulse of the ordinary person.

SUMMARY OF THE ACTION OF ALCOHOL ON THE PULSE.

1. When alcohol or beverages containing alcohol are administered to *healthy* persons in small doses, or even in such doses as will produce transient psychical changes, no alteration of the *pulse rate* is usually observed, provided that local irritation in the mouth and stomach is avoided and the indirect effects of the mental action of the alcohol, such as bodily movements, are not allowed to influence the experiment.

2. It is not improbable that in some excitable individuals the cerebral effects of the alcohol and the circumstances of its administration may combine to induce such mental effects that slight changes in the pulse rate occur.

3. As a rule, when the quantity of alcohol administered is not too small, the *character* of the pulse wave undergoes a slight change, that is, the pulse becomes fuller and softer in consequence of a dilatation of superficial arteries. The heart is not weakened at this time, and the fuller pulse may give a false impression and lead to the belief that the arterial tension has been raised. The pulse tracings of Marvaud, Parkes, von Jaksch, Jaquet, and others show that moderate quantities of alcohol influence the form of the pulse wave in like manner with chloral and other hypnotics, though less markedly from a quantitative point of view. The slight dilatation of the superficial arteries is due to the sedative action of the alcohol on the

vasoconstrictor centre of the medulla. If muscular movements are avoided, the blood pressure remains practically unaffected by small quantities of alcohol. This and other points will be taken up more at length in succeeding sections.

4. The term "circulatory stimulant" is allowable only when used in a popular way, or when it is meant to convey the idea that alcohol can influence the vascular apparatus in one way or another by virtue of an irritating action on mucous surfaces or of a sedative action on the brain.

2. ON THE ACTION OF ALCOHOL ON THE HEART ITSELF.

We have seen that alcohol has little or no effect on the pulse rate of healthy persons when it is so administered that local irritation is avoided. It has, nevertheless, been held to affect the heart itself, some holding that this organ is weakened, others that it is fortified or strengthened by alcohol. It is evident that the question can only be settled by experiments on the "isolated" heart, that is, on this organ separated from its controlling nerves.

The classical research of Martin and Stevens stands without a rival in this field. These investigators experimented on the action of ethyl alcohol on the "isolated" heart of the dog. The details of Martin's method cannot be entered upon here; suffice it to say that the lungs are retained in connection with the heart, and that they are ventilated with the help of an artificial apparatus which keeps the blood that is supplied to the heart sufficiently arterialized. As there are now other methods of isolating the mammalian heart, Martin's method is referred to as the Cardio-pulmonary method. It is sufficiently accurate for all those physiological experiments on drugs in which no account need be taken of vasomotor changes in the lungs. Its adaptability to the investigations of the kind now to be described has lately been demonstrated again by the researches of Bock.

Martin and Stevens found that "when defibrinated blood containing one half of one per cent. by volume of ethyl alcohol is supplied to an isolated dog's heart which has been hitherto working with uniformity, the invariable result is a very rapid and marked diminution in the work done (indicated by the quantity of the blood pumped out from the left ventricle) by

the heart in a given time. When the blood contains only one fourth of one per cent. of alcohol the result is, in most cases, the same; but sometimes it is little or none. After the action of the alcohol has been fully manifested, the heart can in many cases be restored to its original working state if supplied with defibrinated blood containing no alcohol. Blood containing but one eighth of one per cent. of alcohol exerts no influence upon the work by the heart, at least for several minutes." Under the influence of larger and poisonous doses it was found that the ventricular cavity is not obliterated at the end of the systole — the heart, in other words, is overdilated and nearly fills the pericardiac cavity; and during the diastole it has, as a consequence, but little opportunity to dilate and receive a fresh supply of blood, and as a necessary result the quantity of blood pumped round by the organ is greatly diminished.

In a second paper (1883) Martin says, "We have made a few experiments to see what doses of alcohol given by the stomach to a dog will produce some similar action on the heart. When the heart lies in the body and in connection with the central nervous system there are, of course, considerable difficulties to be overcome; and all we can say as yet is, that to get any direct influence on blood pressure one must put much more alcohol into the stomach than an amount equal to one fourth per cent. of the total blood of the animal. It is either not absorbed fast enough to reach at any moment the heart-poisoning limit, or more probably is picked up by other organs, very likely the liver, and held back from the heart.

"We then tried in another way, by directly injecting into the jugular vein of a curarized dog a small quantity of salt solution containing an amount of alcohol equal to one fourth per cent. of the total blood of the animal reckoned as one thirteenth of the weight. In such cases we found, usually, a very temporary enfeeblement of the heart, indicated by a lower arterial pressure; but this seems only to last while the injected solution is flowing through the organ or for a few seconds afterwards. Before the blood returns it has apparently deposited its alcohol elsewhere in the body, or at any rate got rid of it somehow, so that it no longer acts immediately on the heart, at least not to any noticeable extent."

It is apparent, then, that when the blood passing through the

heart steadily contains one half of one per cent. of alcohol, the organ quickly becomes unable to do its work; when the quantity of alcohol becomes less the heart is less affected, and when the percentage reaches only one eighth of one per cent. it exerts no influence, at least not for some time.

Martin failed to give practical significance to these results because he did not analyze the blood of animals to whom alcohol had been administered by the mouth and thus find the actual percentage of alcohol in the blood necessary to produce such and such symptoms.

The researches of Gréhant, which appear to have been unknown to Martin, throw light on the question as to how much alcohol must be taken by the stomach to produce the effects noted by Martin in his "isolation" experiments. Gréhant injected into the stomach of a dog weighing ten kilograms alcohol of forty six per cent. by weight in doses of 93.2 grams at varying intervals during a period of about seven hours. Four of these injections into the stomach were made at half-hour intervals. Three hours later four more injections were made. Ten minutes after the last injection the animal succumbed to respiratory paralysis, though the heart was still beating weakly at the time. Immediately after death, blood from the inferior vena cava was analyzed and was found to contain one per cent. of alcohol.¹

It is safe to assume that a smaller quantity of alcohol would have sufficed to kill this animal, which had received the enormous quantity of 745.6 grams, or twenty-five ounces, of a forty six per cent. solution of alcohol, equal in strength to whiskey.

Gréhant had previously shown that when an animal is in a state of profound intoxication its blood contains only 0.5 per cent. of alcohol. The amount of forty-six per cent. alcohol required to produce this state of deep narcosis in a dog weighing forty-three kilograms was 462 grams, administered in two doses at intervals of half an hour. A man of average weight, say seventy kilograms, would have to take 752 grams, or about over a pint and a half of whiskey, an amount that would be fatal to many individuals, if taken in this short space of time.

From the results of Gréhant it is evident that *very large*

¹ Of course no account is taken of the alcohol that has disappeared in consequence of oxidation and excretion.

quantities of alcohol must be taken into the system in order that the conditions which obtained in the experiments of Martin and Stevens may be realized. In order that the blood may, for a time at least, contain one eighth of one per cent. of alcohol, an individual weighing 150 pounds would have to drink approximately six ounces of whiskey in a short time, say in the course of an hour. It will be admitted by most toxicologists that a single indulgence of this kind would not depress the heart itself more than was found to be the case in Martin's experiments (one eighth of one per cent. in the blood), which are therefore in fair accord with evidence of practical experience. In these experiments, too, the heart did not have the assistance of the thoracic aspiration of the closed chest cavity, nor was there that constant and steady fall in the content of alcohol in the blood which goes on when the experiment is made on the entire animal.

The experiments of Hemmeter (1889) on the action of the various alcohols of the methylic series on the isolated dog's heart substantiate in every particular the results of Martin and Stevens. Hemmeter found, for example, that when the blood supplied to the heart contained one fifth of one per cent. of ethyl alcohol there resulted an average reduction of 17.45 c. c. in the amount of blood pumped round by the heart in thirty seconds.

The very recent experiments of Bock (1899) on the action of various poisons on the rabbit's heart also support Martin's conclusions in every respect. This writer uses the cardiopulmonary method of isolating the mammalian heart, though with certain modifications, such as the employment of extract of leeches to prevent coagulation of the blood and the introduction of a peripheral resistance into the arterial circuit. Bock's experiments lead him to state, as others before him have done, that alcohol in even considerable quantities has no particular influence on the work of the heart.

As further evidence that small doses of alcohol have no direct or immediately harmful action on the heart, a ventricular tracing published by Cushny in his recent work on pharmacology might be put in evidence. This tracing shows that when 8 c. c. of fifty per cent. alcohol is injected into a vein no visible effect whatever is produced in the movements of the heart.

Somewhat larger quantities of alcohol, as 20 c. c. of a fifty per cent. solution, weakened the systole of the auricle in a marked degree and that of the ventricle only slightly.

It is to be remembered, however, that in this form of experiment the alcohol comes into contact with the heart in a degree of concentration which it is impossible to state in terms of percentages.

In respect to the action of alcohol on the mammalian heart, we have thus far found no evidence that it acts as a stimulant for this organ. The most that we are able to say is that moderate quantities, that is, such as do not lead to intoxication, have no direct action on the heart worth speaking of.

The more reliable of the experiments that have been made on the action of alcohol on the heart of cold-blooded animals also fail to give support to the old notion that alcohol is a direct stimulant for the heart.

The experiments of Umpfenbach (1881) deserve brief mention. This investigator exposed the heart of the frog to the action of a little vapor of alcohol and registered its contractions by means of a small lever connected with it. He observed a steady decline in the rate of heart beat after exposure to the vapor of alcohol, and also a change in its character. The curve of the heart beat was at first in the form of a steep and pointed wave, and as the heart began to lose its contractile power it took on the character of a long and low wave, in which the diastole followed only slowly upon the systole. In only one instance did Umpfenbach notice a very insignificant increase of the pulse rate, and he attributed this to unknown and secondary causes.

This writer deserves recognition as being one of the first to point out that, when the administration of alcohol causes an increase in the rate of the heart's beat, the cause for this must not be sought in the direct action of the alcohol on the heart, but in its local action on sensory nerves, in consequence of which the heart is reflexly influenced, or in some other indirect influence of the alcohol.

The work of Ringer and Sainsbury (1883) on the relative effects of certain members of the ethylic alcohol series makes use of more modern methods. These authors employed the instrument known as Roy's tonometer and used a solution of dried bullock's blood, diluted with a normal saline solution, as

a nutrient medium for the heart. Their conclusion is that methyl, ethyl, propyl, butyl alcohol, etc., "by their direct action on the cardiac tissues (frogs' ventricle), are clearly paralyzant, and that this appears to be the case from the outset, no stage of increased force of contraction preceding."

Maki (1884), who studied the effects of alcohol and other drugs on the frog's heart with the help of the perfusion apparatus of Williams, concluded that its contractions become more vigorous and more rapid under the influence of alcohol. The manometer attached to the apparatus also showed a slight rise of pressure. These experiments were made in Professor Schmiedeberg's laboratory in Strassburg, but none of the researches that have since then emanated from this laboratory, such as those of Dreser and Diballa, have corroborated Maki's results. Maki's experiments on the action of alcohol on the heart of warm-blooded animals did not lead him to conclude that alcohol is a direct heart stimulant.

Dreser (1888) has published a valuable work on the action of alcohol and other drugs on the frog's heart, as studied with the help of Williams's apparatus. It may be remarked that this apparatus enables the experimenter to keep the ventricle of the heart under quite normal conditions; it enables him to "perfuse" the heart with diluted blood, or some other nutrient medium, to which a drug may be added. When the influence of the drug has been noted it is easy to wash out the heart with fresh blood and thus restore it to its original condition. Changes in the rate and character of the heart beat, alterations in the amount of work performed by the heart in a given time, and any change in its "absolute power" may all be studied with the help of this instrument.

Dreser has shown that alcohol in small doses, say 0.33 per cent. in the blood, is practically without effect on the frog's heart; only in one experiment with this strength of alcohol did he note a very temporary and unimportant increase in the absolute power of the heart.

In any considerable doses, however, alcohol acts as a direct paralyzant of the heart. Dreser concludes that "the favorable action on the heart attributed by many physicians to alcohol has probably no connection whatever with a direct action of this agent on the heart muscle itself."

Dreser's conclusions are supported by the researches of Diaballa (1894), who has studied in a quantitative manner the action of alcohol and other narcotics of the chloroform group on the rate and height of the pulse and on the "diastolic" pressure. This observer has found that 0.144 per cent. of alcohol, or a little more than one seventh of one per cent., is the upper limit of the amount that can be contained in the blood without injuring the frog's heart.

Any amount above this always has a depressant action on the heart, though this may not be apparent for some time unless the solutions are quite strong, containing, say, from two to four per cent. of alcohol. The deleterious action of the alcohol is always manifested by a decrease in the size of the pulse, although the pulse rate may be but little diminished.

Castillo (1880), Eagleton, and Cerna have published experiments on the action of alcohol on the frog's heart, which are worthless because of a defective method. These investigators do not make use of a nutritive solution to keep the heart in a normal condition, but place an excised heart directly into alcoholic solutions containing from 0.25 to two per cent. of alcohol and compare its rate of beat in these solutions with that observed when the heart is placed in a physiological salt solution.

Castillo finds that in solutions containing from one to two per cent. of alcohol the heart showed an increased frequency of beat lasting from three to ten minutes. Eagleton finds that "in solutions containing 0.25 per cent. of alcohol but little effect upon the pulse rate is observed;" and Cerna concludes that a very dilute solution of alcohol (0.1 per cent.) has no perceptible action upon the frog's heart, but that stronger solutions (0.5 to two per cent.) do increase the rapidity of the beat.

All of these writers are adherents of the view that alcohol in small doses is a cardiac stimulant. Not one of them has paused to consider what would be the condition of a human being whose blood contains from 0.5 to one per cent. of alcohol. We have seen that when the blood contains these percentages of alcohol the individual is in a condition of profound intoxication. Their experiments have been frequently cited in support of the opinion that alcohol is a direct cardiac stimulant, an opinion no

longer tenable in view of the fact that these experiments violate every rule of experimental pharmacology.

As we shall see later, a number of both earlier and later investigators have attempted to controvert the proofs of the inability of alcohol to stimulate the heart directly; that is, to increase its power to perform work, not by carefully repeating the experiments on which these proofs rest and pointing out errors, but by means of deductions drawn from faulty blood-pressure experiments. That the experiments of these writers lead to a very different conclusion from that entertained by them will be pointed out in a later chapter.

SUMMARY AS TO THE ACTION OF ALCOHOL ON THE ISOLATED HEART.

Alcohol in small and moderate quantities, that is, in such amounts as are likely to be found in the blood in any condition far short of intoxication, does not have a direct stimulating action upon the heart; indeed these quantities show no appreciable action for the heart itself, either in the way of stimulation or of depression. This statement refers not to the long-continued administration of small and moderate quantities of alcohol, but to its administration during brief periods of time, as in the experiments cited, and it assumes perfect health of the heart and other organs to begin with.

This conclusion is in accord with the experiments on the pulse already cited and will also be found to harmonize with the physiological data that will be furnished later, when the action of alcohol on the blood pressure is considered.

In very large quantities, such, for example, as result in helpless and perhaps fatal intoxication, alcohol is seen to be a direct and powerful depressant for the heart, weakening first the auricular, later the ventricular systole, causing more or less distension of both cavities, marked slowing of its movements, and great diminution of its output of blood.

The remarks that were made in the preceding summary in reference to the popular use of the terms circulatory and cardiac stimulant apply here also.

The frequent and beneficial use of alcohol in medical practice as an analeptic (stimulant) in conditions of great depressions of the heart and central nervous system do not in the least dis-

prove the positive statement just made that alcohol once incorporated in the blood is not a cardiac stimulant. In the medical cases referred to we are not dealing with the heart alone, removed from all vital connection with the rest of the body. The heart and the vascular apparatus as a whole are capable of being influenced in a *reflex* manner by this many-sided agent, and indirectly also in consequence of the action of alcohol on the central nervous system.

III. DIRECT ACTION OF ALCOHOL ON THE WALLS OF THE ARTERIES AND VEINS.

In order to understand fully the action of a given drug on the vascular apparatus as a whole, the experimenter must inquire into the action of the drug on the "isolated" vessels; that is, upon the blood vessels severed from their connection with the heart and the central nervous system.

It is often an easy matter to prove by direct inspection of a part, by measurement of the velocity with which the blood flows through a given organ, or by noting the time required for an easily recognized chemical to make the circuit of the body, that a given drug has caused a dilatation or contraction of the blood vessels. Experiments of these kinds have been made with alcohol, and while they all point to the conclusion that alcohol in a certain quantity will dilate the peripheral arteries, they do not prove conclusively how this dilatation is brought about, whether it be by an action of the alcohol on the medullary centres controlling the calibres of the vessels or by a direct local action on the walls of the vessels. This point can only be settled in most instances by making "perfusion experiments."¹ These experiments consist in passing defibrinated blood through the blood vessels of a cold-blooded animal whose central nervous system has been destroyed and whose heart is shut out of the circulation. Sometimes an organ, such as the kidney or an extremity of a warm-blooded animal, is used as the object to be "perfused." The details of these experiments and the precautions that must be observed in their execution cannot be described here. Suffice it to say that the whole experiment

¹ For a consideration of the value of the evidence which is obtained by section of the upper part of the spinal cord, consult the section on the action of alcohol on the blood pressure.

consists in forcing arterialized blood under a known pressure into an artery, in measuring the outflow from a vein, and in comparing the normal outflow with this pure blood with that obtained when the blood plus the drug has dilated the vessels.

Kobert has tested the direct action of alcohol on the walls of the blood vessels in such perfusion experiments made with the foot of a calf, and his results are given in the following table:

Amount of alcohol in a thousand parts of blood perfused.	Time of the observed perfusion in minutes.	Alterations in the velocity of outflow in percentage.	Amount of alcohol in milligrams perfused during the experiment.
1	15	8	40
1	10	0	60
2	11	.5	72
2	13	0	98

In four experiments, therefore, an increased outflow of blood was observed but once. Kobert himself refers to his results in the following words: "Alcohol and chloroform do not influence the velocity of outflow in any noteworthy degree. A fall in blood pressure is only observed after large doses of these agents, and then evidently has its cause in their action on the vasomotor centre."

It may then be asserted that small and moderate amounts of alcohol have no direct action on the walls of the blood vessels. Very large amounts no doubt have a direct dilating action on the vessels like that shown for the heart itself. The flushing of the face and other parts of the body, so frequently observed after moderate quantities of alcohol, is brought about by an action on the nervous mechanism which controls the calibre of the vessels. The nature of this action will be discussed at length in the following section.

IV. INFLUENCE OF ALCOHOL ON THE ARTERIAL BLOOD PRESSURE.

On examining into the action of any substance on the blood pressure it must be borne in mind that the pressure of the blood in the arteries is a resultant effect of the work of the

heart and of the peripheral resistance offered by the blood vessels. These are variable factors. Both heart and vessels may be directly influenced by drugs, and both may be affected through their controlling nerves if the drug acts either on their central or peripheral connections.

It is well known that minor fluctuations in the arterial pressure are of frequent occurrence, and Hensen even affirms that daily changes of 40 to 60 mm. Hg. are not uncommon in individuals lying in bed. Arterial pressure, as usually measured, indicates only the lateral pressure on the walls of the larger arteries, and without additional data it gives us no information on that important question, the intensity of the blood flow; in other words, the amount of blood which passes in the unit of time through a given capillary area. Whether an organ will receive its required amount of oxygen and other necessary material must all depend on this. Now the state of constriction of the peripheral arterioles is a factor of the greatest importance in determining the value of this resultant as well as of the arterial pressure. As Krehl, Hensen, and others have pointed out, even during periods of little or no variation in the aortic pressure considerable variations are possible in the unit quantity of blood passing through the aorta. In other words, variations in the peripheral resistance may be offset in such a way by responsive variations in the action of the heart that a change occurs, either in the way of an increase or decrease, in the amount of blood passing through the organs of the body, although aortic pressure remains practically unchanged. As a rule, an increase in arterial pressure means an increase in the intensity of the peripheral circulation. Being an important item in the study of hæmodynamics, blood pressure determinations cannot be neglected, yet it is necessary to point out, as Hensen has well said, that what we most need to know is not the arterial blood pressure, but rather the relation of the quantitative blood flow in any given organ to the actual needs of that organ, a relation which at present it is impossible to determine.

In studying the influence of alcohol on the blood pressure, the use of anæsthetics such as chloroform and ether has often been avoided, on the ground that these substances tend to depress the heart and the nerve centres controlling the circula-

tion, and thus to interfere with and hide the true action of alcohol.

Again, it is very desirable in experiments of this kind to have the muscles of the body removed entirely from voluntary or reflex control, in order that the disturbing influence on the circulation of changes in the respiration, etc., may be avoided. Curare is the agent usually employed to "immobilize" the animal experimented on. Its use involves certain precautions. Only a few of the experimenters about to be cited have employed this drug.

Occasionally the spinal cord is severed at its upper end, in order to eliminate cerebral influences on the circulation and on the skeletal muscles of the animal. The significance of the precautions to be observed in this procedure will be referred to at greater length in a later passage.

It is evident that when neither anæsthetic nor curare has been employed in experiments with alcohol on the blood pressure, a multitude of errors due to reflex or voluntary movements, or even to an increased tension of the muscles not noticeable to the experimenter, may vitiate the results. This is true more especially of those experiments in which the effect of small quantities of alcohol is studied.

But in spite of the fact that there is a great diversity in the methods that have been adopted by experimenters in their study of the action of alcohol on the blood pressure, and that contradictory results have been obtained in reference to the action of *small* quantities of alcohol, we shall nevertheless be able to arrive at correct conclusions on this point. To do this it will only be necessary to study the writings of those experimenters who have employed the best methods and have most judiciously estimated the various sources of error.

If we examine the work of those who have attempted to make their experiments coincide most nearly with the conditions of actual life, and who have, therefore, made no use of an anæsthetic, of curare, or of other similar experimental procedures, we must give high rank to Zimmerberg (1869), whose work on the influence of alcohol on the pulse has already been reviewed. This investigator gives a number of protocols of experiments in which the alcohol was introduced, not into a vein, but into

the stomach. The following is a part of the protocol of one of these experiments:—

Experiment I. Cat of average size. 60 c. c. of forty per cent. alcohol (by volume) injected into the stomach.

Time.	Blood pressure.	Pulse in 10 sec.	Remarks.
	188 mm. Hg.	46	Blood pressure before alcohol varies from 184 to 192 mm.
H. M. 0.00	Injection of the alcohol.		
0.02	190	46.5	Movements.
0.06	184	42	
0.11	186	40.5	
0.16	184	41	
0.21	178	36.5	
0.26	149	38	
0.27	144	38	Reflexes present, but weak.

In a second experiment the same quantity of alcohol was injected into the stomach of a large cat, and with a similar result, except that the fall in the blood pressure did not occur so quickly.

Now, although the amount of alcohol injected was unnecessarily large, it must be remembered that the alcohol was not thrown directly into the circulation. If alcohol has power to raise the blood pressure, the influences of local irritation in the stomach being barred out, a rise of blood pressure might well be looked for during *the first few moments of absorption*. This is not the case in these experiments. They serve to demonstrate that alcohol may be introduced into the stomach of a cat in quantities sufficient to cause intoxication in less than half an hour without raising the blood pressure. In fact, a steady decline in both blood pressure and pulse rate is observed.

Zimmerberg also administered alcohol in moderate quantities, by injections into the jugular vein. One of his protocols may be cited.

Experiment IV. Cat of average size, 11 c. c. of alcohol, thirty per cent. by volume, injected in three portions into the jugular vein.

Time.	Blood pressure.	Pulse in 10 sec.	Remarks.
	148 mm. Hg.	38.5	Maximum blood pressure 150 mm. Minimum blood pressure 146 mm. Observations continued for one minute.
M. S. 0.00	First injection of 5 c. c. of the alcohol. Time employed in the injection forty-two seconds.		
0.20	150	36	Movements.
0.42	140	31.5	
0.57	138	31	
1.12	144	31	
1.14	Second injection of 1 c. c. of the alcohol.		
1.50	142	29.5	
2.52	162	27	This maximum pressure continued for a short time only and was caused by violent movements on the part of the animal.
3.00	Third injection of 5 c. c. con- tinued during one minute.		
3.20	144	26.5	
3.37	130	25	
4.07	102	22.5	
4.48	128	23.5	
5.07	134	23.5	
5.45	142	23	Reflexes entirely normal.

In this experiment precautions are taken against too much alcohol, and the effects of too great a concentration are almost avoided by injecting small quantities at a time and very slowly.

None of the later experiments in this field, in which no curare was employed, are less open to criticism than this experiment of Zimmerberg. It will be seen that in his experiments no rise of blood pressure occurs *except in connection with muscular movements*. After the third injection a fall in pressure of short duration occurs, due to the direct depressant action of the alcohol on the heart. This organ soon recovers, but as in the other similar experiments of Zimmerberg, the blood pressure does not again quite reach the normal level.

The remaining blood pressure experiments reported by Zimmerberg all bear out the statements already made. Those of his experiments that are intended to prove that large doses of alcohol slow the heart not only by a direct action on its muscu-

lar tissue, but also by stimulating the cardio-inhibitory centre, are open to objections. Experiments of subsequent investigators have shown that in respect to this last point Zimmerberg was wrong in his inferences.

Zimmerberg sums up in the following words that part of his work which modern research has confirmed:—

“If we survey the results of all of our experiments, we find that in all those in which the pulse rate was determined in unfettered animals and in human beings alcohol caused no increase in the frequency of the heart's contractions. These experiments also show that alcohol causes a slight fall of temperature, and finally, in large dose, a lowering of the arterial pressure. In the light of these experiments one is not only justified in denying to alcohol any stimulating power whatever for the heart, but on the contrary, in declaring that it lowers the working capacity of that organ.”

A few years later a Russian pharmacologist, Sjetschenow (1872), is cited as stating that alcohol sometimes leaves the blood pressure unaltered and sometimes raises it. I have been unable to secure the original treatise of this writer, and can therefore offer no remarks on his work.

In 1874 Dogiel stated, in a paper read at a meeting of Russian scientists at Kasan, that the blood pressure is always raised by alcohol in small quantities and lowered only when large quantities are used. A brief aphoristic abstract of Dogiel's conclusions was published in Pflüger's “Archiv” without any experimental details, and nearly all subsequent writers who hold the same opinion have cited this abstract in support of their own view.

An examination of Dogiel's numerous protocols as published in the Polish language in 1878 and 1879 has, however, convinced me that his conclusions are entirely unwarranted and incorrect. Too much stress is laid on a slight rise of pressure, say of 4 mm. of mercury, occurring at the time of the injection. Thus, in one experiment on a dog of average weight, the blood pressure before alcohol was 176 mm. In the course of a little over three minutes, during the first part of which period 30 c. c. of a thirty per cent. solution of alcohol was introduced into the stomach, the following average pressure was noted: 180, 160, 172, 159, 159.

In a second experiment, in which the normal blood pressure was at first 161 mm. and ten minutes later 144 mm., the following values were noted as a result of two injections of 10 c. c. of thirty per cent. alcohol into the jugular vein :

148 (10 c. c. thirty per cent. alcohol), 165, 157, 145, 158, 176 (10 c. c. of thirty per cent. alcohol), 114, 145, 145, 145. These changes occurred in the course of about seven minutes.

In another experiment the normal pressure is given as 108 mm. As a consequence of two intravenous injections of alcohol, the following series of pressures is offered :

114 (12 c. c. of thirty per cent. alcohol), 116, 180, 100, 115, (14 c. c. of thirty per cent. alcohol), 104. In this experiment the jump from 116 to 180 occurred 20 seconds after the injection.

In a fourth experiment the normal pressure was 163 mm. The intravenous injection of 12 c. c. of forty per cent. alcohol gave the following series of pressures : 163 (12 c. c. of forty per cent. alcohol) 172, 144, 144, 145, 158, 139, 83. The time covered by this series is fourteen minutes.

Further protocols, as illustrative of Dogiel's ideas of the action of small doses of alcohol on the blood pressure, need not be cited. It is to be remembered that these experiments were made on non-anæsthetized animals, on all of which the surgical operations necessary for kymograph connections and jugular canulæ had been made, and that slight movements and even struggles on the part of the animal are consequently of frequent occurrence, and often cause just such a sudden rise and fall in the middle of an experiment as is well illustrated in the third experiment cited.

Again, Dogiel gives no countings of the respiratory movements, and thus deprives his critics of valuable data for judging his work. So large a proportion of those among his experiments in which small and moderate quantities of alcohol were injected into the stomach or into the jugular vein either show only an insignificant rise of pressure at the moment of injection, or else such sudden, unexplained, and accidental fluctuations at variable times after the injections, that we are forced to believe that Dogiel has drawn his conclusions to harmonize with preconceived notions. It was an error commonly held in Dogiel's day that alcohol is a powerful vascular stimulant. Properly

analyzed these experiments amply verify the statements of Zimmerberg.

To this same period belong a number of other writings which claim to show that alcohol raises the blood pressure. Lussana and Albertoni (1875) do not agree with the conclusions of Marvaud, Zimmerberg, and others. According to these writers alcohol greatly increases the energy of the heart's contractions at the same time that it dilates peripheral vessels. The result is a rise in arterial tension. Their arguments are based entirely on sphygmographic tracings taken from the radial artery and are worthless when viewed in the light of modern physiology.

The same criticism holds for Marvaud, who tried to make his sphygmograms accord with the conclusions arrived at by Zimmerberg. This writer's conclusions as to the influence of alcohol on the rate of the heart beat have already been criticised in a previous section; as to his other conclusions, though in part correct, they are nevertheless, like those of Lussana and Albertoni, deduced from insufficient evidence.

Ronchi and Salvioli (1875) express opinions, in their *Studio-critico-sperimentale* on the physiological action of alcohol, which are similar to those held by Lussana and Albertoni. Their standpoint is the now untenable one that alcohol stimulates the heart itself, and they point to the increase in the systolic rise of their pulse curves in proof of their assertion. They also believe that their blood-pressure measurements show a rise of arterial pressure after the injection into the stomach of moderate quantities of strong alcohol (43.6 per cent. by volume). But here too we meet the errors into which all those have fallen who have attempted to show that alcohol raises the blood pressure.

The variations in the mean arterial pressure in the experiments of these investigators, both before and after alcohol, were very great. Thus, before alcohol the pressure in a number of experiments ranged from 65 to 85 mm., from 55 to 75 mm., from 68 to 95 mm., from 65 to 90 mm., and so on. In some of the experiments after alcohol the oscillations in pressure are reported as being "irregular and tumultuous," as in one experiment in which twenty grams of a 43.6 per cent. solution of alcohol was injected into the stomach of a small

dog weighing 6.8 kg. In most of the experiments the alcohol used was so strong that it acted as a powerful irritant for the lining membrane of the stomach. A little mustard and water or a little dilute silver nitrate solution would have had, when injected into the stomach, the same effect.

When only small quantities of more dilute alcohol were injected into the stomach the protocols show that only an insignificant rise of pressure occurred ; often there was no rise at all, and sometimes a fall.

Maki (1884) first lowered the normal blood pressure of rabbits by means of intravenous injections of sodium-cuprous tartrate and then injected alcohol. He found that in this case small doses of alcohol, when injected into a vein, caused a very slight rise of pressure. Here we are dealing with a problem in pathology. Maki says that the increase in pressure was very small and was probably dependent on fortuitous circumstances and was not due to a strengthening action of the alcohol on the heart.

A number of American investigators, Castillo, Eagleton, and Cerna, have also appeared to prove that small quantities of alcohol raise the blood pressure. As far as I can gather from their papers none of these writers has studied Zimmerberg or Dogiel at first hand. Eagleton refers to Zimmerberg in the following terms : " His studies, I believe, were made upon animals and were evidently conducted with a view of studying the toxic rather than the therapeutic action of alcohol, as enormous doses of the drug were used ; " and Castillo refers to the brief review of Zimmerberg's work found in Wood's " Therapeutics." ¹

Castillo's paper on the physiological action of alcohol on the circulation appeared in the " Philadelphia Medical Times," vol. xi. (1880-81), page 44, in the form of a brief abstract of an unpublished and inaccessible prize essay. As this abstract contains only categorical statements, without experimental details of important points, discussion of its merits is impossible. This author, however, states that " Alcohol in small doses has no effect, or else causes an increase of pressure, while large doses cause a decrease." He also says, " I attribute both the increase and the decrease (of pressure) to a direct cardiac action, since

¹ Page 361, ninth edition.

it was found that after the isolation of the heart from any centric nervous influence the same changes in pressure still occur; and I found that when the fall of pressure was very pronounced the vasomotor centre and peripheries were still intact." The abstract closes with a series of nine positive statements; as, "that alcohol in small doses causes an acceleration of the pulse with increased cardiac force," etc.

It is to be regretted that the original essay on which the above abstract is based is not accessible, since this abstract itself is cited with approval by Wood, Cerna, and Eagleton, and is thus made to support opinions which cannot stand the test of a close physiological scrutiny.

Eagleton's experiments, like those of Castillo, were performed in the physiological laboratory of Professor Reichert, and his views are in accord with those of Castillo and Reichert. An examination of the protocols of his experiments will not allow the reader to subscribe to his conclusion "that dilute alcohol in small doses, frequently repeated, increases cardiac force and arterial pressure." In Eagleton's experiments alcohol of "about twenty-five per cent." was allowed to flow from a pipette containing 100 c. c. into the external jugular vein, the flow being controlled by means of a screw clamp placed on the tubing that connected the pipette with the vein. This is called the method of continuous injection.

I will give one of Eagleton's protocols in its entirety in order to show how impossible it is to draw such conclusions as he has done.

First Series — Normal Animals.

Experiment No. 1. Dog, 8.173 kilos.

Time. A. M.	Blood pressure.	Pulse.	Resp.	Alcohol 25%.	Remarks.
10.	180	132	15		
10.00 $\frac{1}{4}$	—	—	—	Intravenous injections 5 c. c.	
10.00 $\frac{1}{2}$	170	124	12		
10.00 $\frac{3}{4}$	—	—	—	Intravenous injections 5 c. c.	
10.02	165	124	13		
10.04	—	—	—	" "	
10.09	—	—	—	" "	
10.10	142	108	9		
10.10 $\frac{1}{2}$	—	—	—	" "	

Time. A. M.	Blood pressure.	Pulse.	Resp.	Alcohol 25%.	Remarks.
10.13	148	111	8		Marked inhibitory action of the heart. Struggling and whining. Clot for 4 minutes.
10.15	160	127	14		
10.16	-	-	-		
10.20	-	-	-		
10.21	-	-	-		
10.25	-	-	-	Intravenous	
10.27	140	128	28	injections 5 c. c.	
10.32	135	120	30	Continuous injection started.	
10.37	140	125	30	Has received 36 c. c.	
10.40	-	-	-		
10.43	74	57	5		Blood pressure rapidly falling. Respiration very shallow.
10.43½	-	-	-		Dog died. 5 respirations after heart ceased, at intervals of ten seconds.

As the reader will perceive, there is no evidence here of a rise of blood pressure above the normal which is due to alcohol. A rise such as always follows struggling on the part of the animal is apparent at 10.15, but even then the pressure does not reach the normal level.

Experiment No. 2, which I need not give, also shows no rise of pressure, but on the contrary a steady fall due to the quantities of alcohol continuously injected. Immediately after the beginning of the injection there is an increase in the pulse rate from 147 to 170, very likely of reflex origin.

Experiment No. 3 shows a small rise of pressure of 15 mm. (from 134 to 149 mm.) two minutes after the continuous injection was started, and at a time when the small animal had already received 20 c. c. of the alcohol. This rise occurred in four minutes after the injection was commenced, and at the time of its occurrence the respirations had increased from twenty to twenty-five per minute.

Now it is well known to experimenters that when alcohol is injected with avoidance of irritation at the point of injection it

causes no increase in the respiratory rate of dogs. It is apparent, then, that some abnormal circumstance accounts for both the temporary rise of pressure and the increased respiratory rate, which are noted in this experiment. Two minutes after this small rise of pressure occurred, the reflexes had disappeared, the animal's muscles were relaxed, the respirations had become very shallow, and the blood pressure had fallen to 128 mm. By this time the animal had received 50 c. c. of the alcoholic solution. This experiment, therefore, only illustrates the well-known fact that alcohol in large doses steadily lowers the blood pressure.

In Experiment No. 4 the conditions are only slightly different. Here Eagleton begins by injecting 1 c. c. of "pure alcohol" into the jugular vein, which causes struggling and whining and raises the blood pressure from 131 to 156 mm. in the space of one minute. After this wrong beginning the "continuous injection" of twenty-five per cent. alcohol is started, with the result that the blood pressure, which had fallen meanwhile from 156 to 144 mm., again rises a little after 40 c. c. of the twenty-five per cent. alcohol has been injected. It then falls again (133) to almost the original figure (131). At this time the pulse rate had fallen from 228 to 161 and the respirations had increased from 48 to 50. The next and last of the experiments on normal animals is made on a very small dog of 4 kilos, and deals almost entirely with the results of two injections of *absolute* alcohol in doses of 1 c. c. each. The animal struggles and whines, and the results are of no value.

Eagleton reaches the conclusion that "dilute alcohol in small doses, frequently repeated, increases cardiac force and arterial pressure." As far as I can gather from his discussion of his protocols, he arrives at this astonishing conclusion because, in Experiments 3, 4, and 5 of his paper, "a decided increase in blood pressure was noted immediately after the alcohol was injected."

I have already commented on the temporary rise of pressure observed in Experiment 3, and can merely add to what I have said about Experiments 4 and 5, that the injection of pure alcohol into a dog that struggles and whines proves anything but the assertions made in Eagleton's conclusions. It is

evident, then, that the experiments of Eagleton, when properly interpreted, fall in line with those of Zimmerberg and entirely support such of his conclusions as we have accepted.

The rest of this paper deals with the effects of alcohol after section of the pneumogastric nerves and the spinal cord, with the result that the changes in the pulse remain the same after section of all the nerves going to the heart. Then follow worthless "confirmatory experiments" on the isolated frog's heart placed in solutions of different strengths of alcohol, to which reference has been made in a former paragraph.

We may next examine the work of Cerna, who also affirms that "small doses of alcohol produce increased rapidity of the cardiac beat; large doses, a depression of the same. In either case the effect is brought about mainly by and through a direct cardiac action. The drug in small quantities causes a rise of the arterial pressure by a direct action upon the heart; in large amounts it depresses the arterial pressure similarly through a cardiac influence." Cerna gives the protocols of four experiments on non-curarized animals. The alcohol employed varied in strength from twenty to twenty-five per cent. and was injected into the jugular vein partly in the ordinary way and partly by the method of "continuous" injections.

In the first experiment (Experiment No. X. of the paper) on a dog of 6.12 kilos the blood pressure stood at 150 mm. to begin with, and in thirty seconds after the injection of 10 c. c. of twenty-five per cent. alcohol, for which injection thirty seconds were employed, it had risen to 168 mm. A minute and a half later 15 c. c. was injected, and about two minutes after this 20 c. c. was injected. At the completion of this last injection, and five and one half minutes after the first injection was begun, the blood pressure stood at 154 mm., as compared with the normal of 150 mm., the pulse was 162 as against 148, and the respirations were 18 as against 20. There are no comments as to the muscular movements during this period; later it is remarked that the animal whines and struggles. An animal that is tied down, and that is not receiving anæsthetic, often contracts his muscles in a trial effort, so to speak, without entering upon a struggle sufficient to attract the experimenter's attention. Such a tense condition of the muscles always causes minor variations in the blood pressure. That alcohol causes a

condition of muscular unrest is well known to modern workers on the subject of the respiration.

If Cerna had given a protocol of the blood pressure, pulse rate, etc., of this same animal, for say, a half hour before giving alcohol, he would undoubtedly have observed variations similar to those attributed by him to alcohol. And yet this Experiment No. X. is that one of the series of four which I am now discussing which is best adapted to support Cerna's conclusion.

In Experiment No. XI. the rise of pressure amounts to 5 mm. only, except at one period when it reaches 188, the normal being 175.

In Experiment No. XIII., the third of the series with dilute alcohol, the normal pressure is 132, the pulse 140, the respirations per minute 24. The operation of preparing the vagi has been made. The method of continuous injection is used. This time it requires five minutes to raise the arterial pressure from 132 to 138 mm., a rise which may be disregarded under the circumstances. The greatest rise noted is only 12 mm. Inside of twenty minutes the small animal weighing 8.3 kilos has received directly into the circulation 155 c. c. of twenty per cent. alcohol (!), and at this time the arterial pressure still stands at 128 mm., the pulse rate is 132, the rate of the respiration 18.

In the last of this series of four experiments the greatest rise of pressure noted is only 6 mm. (from 138 to 144 mm.), and it requires two minutes and twenty seconds to attain this rise.

Considering that Cerna has made use of non-curarized and non-anæsthetized animals, and that the observed rise in blood pressure is not at all noteworthy, that it sometimes appears immediately after the injection but more usually at varying intervals after, and remembering that minor variations, such as a rise of from two to five or 10 mm., have no significance when they occur in non-anæsthetized animals on which operations such as fitting the syringe to canulæ, etc., have been performed, no one will be prepared to believe that the rise of blood pressure and the increased pulse rate observed by Cerna are caused by the alcohol as such.

Cerna also gives the protocols of two experiments on curarized dogs, but singularly enough, in these experiments, he uses

only *absolute* alcohol in doses of 1 and 2 c. c. In the second of these experiments the greatest rise is only 4 mm., a quantity too small to be considered; in the first the greatest rise obtained is 10 mm., and occurs eight and one half minutes after the completion of the injection of absolute alcohol, and is no doubt due either to imperfect curarization or to an after effect of the irritation of the alcohol in the veins or in the heart itself. As to the pulse rate in these experiments, this goes up and down, in the second experiment, in the times between the successive injections, being now above and now below the normal rate, so that it becomes impossible to suggest an explanation for this remarkable behavior.

Similarly, the two experiments (Experiments Nos. XX. and XXI.) made on animals with the spinal cord severed and the vagi cut, do not prove what they are supposed to do. In the first of these experiments a rise of pressure from 88 to 102 mm. is noted as following on the injection of 2 c. c. of *absolute* (!) alcohol, but this rise does not occur until some minutes after the injection is completed and is never seen in the subsequent injections. That it is not allowable to inject undiluted absolute alcohol will be admitted by all experimenters without further comment.

A similar tardiness in the rise of pressure is shown in the second experiment. If the rise of pressure imputed to the alcohol finds its explanation in the action of this agent on the heart, as Cerna maintains, it is not easy to see why the heart should respond so slowly to the stimulating action of the alcohol when it is, so to speak, thrown directly into that organ.

In regard to experiments on the circulation made after section of both the spinal cord and vagi, it must be borne in mind that an asphyxial rise of pressure is possible if the artificial respiration be carried on imperfectly, as shown in the work of Ustimowitsch, Kowalewsky, Adamük, Konow, and Stenbeck; and also that a small reflex rise of pressure is still possible, as has been clearly proved by the researches of Bochefontaine, Smirnow, and Ustimowitsch.

The inferences which Cerna has drawn from that part of his work which deals with the action of small quantities of alcohol on the circulation are untenable. When his protocols are properly edited they prove just the opposite from what is main-

tained by him; namely, that small quantities have no appreciable influence on the blood pressure. Gibbs and Reichert also state that alcohol in small doses increases the arterial pressure and the frequency and force of the heart beat. No protocols are given by Reichert; and if protocols had been furnished they would undoubtedly have been similar to those of Eagleton, which emanated from his laboratory the year before Gibbs and Reichert's paper appeared.

The views that have thus far been upheld — namely, that small and moderate quantities of alcohol do not cause a rise of blood pressure — find ample support in the opinions and work of Gutnikow. This writer has shown that when strong solutions of alcohol are thrown into the stomach a temporary rise of blood pressure always precedes a fall, and that the observed rise is due to the local irritating action of the alcohol on the walls of the stomach.

This investigator used only curarized animals. The much discussed question of the influence of curare on the blood pressure and on the irritability of the end organs of the vasomotors cannot be entered on here. We need not, however, declare, as Cerna has done, that Gutnikow's experiments lose much of their value on account of the use of curare. Tillie has shown that the dose of pure curarine required to paralyze the vasomotor nerves is from 100 to 300 times as large as the amount required to produce complete paralysis of the skeletal muscles; therefore it is plain that the amount used in the experiments cited is too small to have any effect on the vasomotor nerves.

A later paper by Pick also traverses this whole field of controversy and shows that curare in the proper doses does not appreciably influence the blood pressure nor alter the excitability of the vasomotor nerves. Hunt, moreover, has shown that a reflex rise of blood pressure is produced more easily in a curarized than in an uncurarized animal by the irritation of a sensory nerve; hence it is very probable that the curare employed by Gutnikow increased rather than decreased the tendency of the alcohol to cause a reflex rise of pressure.

Gutnikow injected large quantities (200 c. c.) of strong alcohol (fifty to seventy per cent.) into the stomachs of curarized dogs. In all of his tables it is noted that a more or less marked rise of blood pressure follows *immediately* upon the injection

of the alcohol as its first effect. This rise is properly referred by this investigator to the reflex effect of the caustic action of the alcohol. He produces a similar rise by injecting a ten per cent. solution of silver nitrate. In this case the preliminary rise is soon followed by a fall of pressure, and Gutnikow is inclined also to attribute a part of this fall of blood pressure to reflex action, although stating clearly that he attributes only a minor rôle to this cause.

In this connection it may be of interest to note that Hermann, Sigmund Mayer, and Przibram have shown that merely filling the stomach with non-irritating fluids, such as water, may cause a rise of blood pressure.

Gutnikow makes no experiments to prove that alcohol in small doses raises the blood pressure in any other than in a reflex manner, but accepts it as a proved fact that it can only lower the pressure when it reaches the circulation without causing local irritation on any part of the surface of the body. Aside from the points already abstracted, his paper has no bearing on the points now under discussion. The object of his paper is to harmonize the fact that alcohol lowers the blood pressure with the equally well-known fact that it is used in medical practice as an analeptic or "circulatory stimulant," as an agent that "strengthens and fortifies the heart."

It would take us too far afield into the subject of the mechanics of the circulation to discuss Gutnikow's conclusions and experiments. Suffice it to say that he believes that the propelling power of the heart is not injured but rather improved by alcohol, and that this is a consequence of its having altered the mutual relations of the pressure in the cavities of the heart and in the arteries and veins. The sum total of the action of alcohol on the circulation, according to Gutnikow, is to the effect that although there is a condition of lowered arterial blood pressure due to a vascular dilation which is caused by a sedative action of the alcohol on the vasoconstrictor centre, yet in consequence of the peculiar relative distribution of pressures in the various parts of the circulatory apparatus, *the heart works as if it were strengthened*; it has an easier task in keeping all the small arteries, veins, and capillaries of the body well filled.

It is perhaps unnecessary to offer further evidence in support

of the assertion that the arterial pressure is not raised by alcohol, and that the exceptional occurrence of a rise of pressure can always be explained as the result of a failure to observe certain experimental precautions. My own experience during the past ten years coincides entirely with that of Zimmerberg, Dreser, Diaballa, and others, whose work in the present review has been accepted as highly trustworthy.

The following experiments, which were made recently in my laboratory, are given in illustration of my own observations. In these the necessary operations were performed under anæsthesia with ether or chloroform. After all the connections with the kymograph, respiration tambour, injecting burette, etc., were made, the ether flask was disconnected from the tracheal tube and the alcohol was admitted into the vein after the blood pressure had come to a fairly permanent level. It need hardly be mentioned that such experiments are best performed in a quiet room, and that once the instruments are in place all handling of the animal should be avoided. The burette from which alcohol warmed to $37\frac{1}{2}^{\circ}$ C. is allowed to flow into the femoral vein is joined to the venous canula by means of a sufficiently long piece of soft rubber tubing, so that the alcohol can be turned on without the slightest pull on the vein or irritation of the wound. It will be noted that alcoholic solutions of varying strength were employed. In my own opinion solutions of ten per cent. by volume are quite strong enough to serve as a test of the blood-pressure raising power of alcohol. Stronger solutions only serve to introduce disturbing factors. Nevertheless I have made use also of such solutions out of deference to those who have employed them in their own experiments.

At first, except in Experiment III., the alcohol was admitted to the circulation while the animal was still in a state of light after-anæsthesia, and it was hoped that later the alcohol itself would act in some degree as an anæsthetic. If it be asserted that all degrees of anæsthesia vitiate the experiment and that alcohol can only raise the blood pressure when the vasomotor centre is not in the least under the influence of a narcotic, it may be replied that in this case alcohol must indeed be a feeble vascular stimulant, since all other stimulants are quite able to manifest their power under the above-named conditions.

Experiment I. July 5, 1900. Female dog, weight, 5900 grams.

At first alcohol of ten per cent. by volume was allowed to flow slowly from a burette into the femoral vein, and later a specimen of port wine obtained from the Johns Hopkins Hospital was used in place of the alcohol. The respirations were registered from an abdominal tambour.

Time p. m.	Mean arterial pressure (carotid artery) in mm. Hg.	Respirations in ten seconds.	Alcohol, ten per cent. by volume. Port wine.	Remarks.
H. M. S.				
12 12	146			
12 13	136			
12 13 43	141		Alcohol turned on.	
12 14 03	125		Alcohol cut off. Quantity, 1 c. c. Time of injection, twenty seconds.	Respiration rapid.
12 15	124			
12 16 10	135		Allowed to flow.	
12 17	146		Cut off flow. Quantity, 11.8 c. c. Time of injection, fifty seconds.	
12 19	143			
12 20 24	143		Alcohol again.	
12 21 39	148		Alcohol cut off. Quantity, 15 c. c. Time of injection, seventy-five seconds.	
Dog again receives ether while tracing pens are being arranged, but ether is removed at 12.38'20".				
12 38 20	143			
12 40 05	141			
12 41 09	152	35	Alcohol again turned on.	
12 42 09	144	33	Alcohol still flowing.	
12 43 10	144	35	Alcohol still flowing.	
12 44 10	140	38	Alcohol flowing faster.	
12 45 10	140	34	Alcohol still flowing.	
12 45 40	136	45	Alcohol cut off. This time 19.9 c. c. injected in four minutes thirty-one seconds.	
12 46 40	136			
12 48 20	138	34	Alcohol turned on.	
12 49 20	134	28	Alcohol still flowing.	

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Time P. M.	Mean arterial pressure (carotid artery) in mm. Hg.	Respirations in ten seconds.	Alcohol, ten per cent. by volume. Port wine.	Remarks.
H. M. S.				
12 50 20	130	37	Alcohol still flowing.	
12 51 20	126	35	Alcohol cut off. This time 53 c. c. injected in three minutes.	
12 52 20	128	30		
12 53 20	131	29		
12 54 20	127	27		
12 55 20	128	32		
12 56 10	128	34	Port wine from burette.	
12 56 38	112	36	Injection ended. 7.5 c. c. in twenty-eight seconds.	Pressure shows rapid, sudden fall with quick return when wine is removed.
12 57 48	138	34		
12 57 48	138		Port wine again.	
12 58 55	131	30	Injection ended. 7 c. c. in sixty-seven seconds.	No sudden fall of pressure this time.
12 59 55	132.6	28		
1 02 05	135	34	Port wine again.	Sudden fall in pressure.
1 02 25	90	36	Port wine continued.	
1 04	92	30	Port wine cut off. 30 c. c. injected in ninety-five seconds.	
	Pressure now remains low with wide, irregular excursions of the manometer, suggesting a vagus effect.			
1 07	79	18		Both vagi cut.
1 10 48	142	25	Port wine again.	Again sudden fall, then slight rise.
1 11 58	116	28	Port wine continued.	
1 12 58	78	20	Port wine cut off. 18.3 c. c. injected in two minutes.	Wide excursions of the manometer appear again. Heart beats grouped. Gradual improvement until curve again becomes normal.
1 13 58	76	13		
1 18 58	135	21		

In commenting on this experiment I would call attention to the slight fall of pressure (10 mm.) that occurred immediately before the alcohol was allowed to flow into the vein; also to the rise that occurred from unknown causes between 12.40 and 12.41. Similar irregularities, either in the direction of a rise or fall, are seen frequently in all experiments in which the anæsthesia is not too deep. The first injection of but little more than 1.1 c. c. was followed immediately by a fall of pressure which surely cannot be laid to the charge of the alcohol. The second injection, 11.8 c. c. in the space of fifty seconds, was followed by a rise of 11 mm. After a pause, during which the animal again received ether, a similar rise was not observed even where the arterial pressure was at the normal level when the injection was made. I look upon such variations of the arterial pressure as not due to a direct action of the alcohol, because they are as likely to be in a downward as in an upward direction and occur also in lightly anæsthetized animals when no drug is injected. As more and more alcohol was allowed to enter the blood, the circulatory apparatus became less irritable, and from 12.41'09" to 12.51'20" we observe the typical action of dilute ethyl alcohol when injected slowly, — that is, its effect is a slow and progressive fall of blood pressure, as in the case of its pharmacological congeners, ether, chloroform, etc.

Small quantities of port wine had no effect, while moderately large quantities caused a marked lowering of the pressure and slowing of the respiration, with great weakness and irregularity of the heart's action, due partly to the harmful action of some constituent of this wine other than ethyl alcohol.

Experiment II. Small dog. Chloroform used as the anæsthetic both during the surgical operation and the subsequent injection of the alcohol (ten per cent. by volume).

Time P. M.	Mean arterial pressure in mm. Hg. (carotid artery).	Pulse rate per minute.	Respirations per minute.	Remarks.
H. M. S.				
3 12	65	126	60	
3 12 23	65	126	60	Began injection from burette into right femoral vein.
3 12 58	67	132	60	Has received 10 c. c.
3 14 53	58	132	54	Has received 20 c. c.
3 15 23	56	132	54	Has received 25 c. c.

In this experiment no appreciable rise of pressure occurs. The animal was small and in poor condition, and the abnormally low blood pressure is not to be attributed to the chloroform. In a second instance, an animal also under chloroform with a blood pressure of 150 mm., an injection of 12.5 c. c. of ten per cent. alcohol in fifty-one seconds had practically no effect, the pressure falling to 148 mm. Whiskey diluted with an equal volume of water also had no other action than to cause a slight and progressive lowering of the pressure.

Experiment III. Dog weighed 20 pounds. At 9 A. M. 200 c. c. of blood taken from the carotid artery under ether anæsthesia. Was allowed to rest, tied with a rope, so as to have liberty to move about, until 2.30 P. M. At 3 P. M. the necessary connections had been made and the animal was ready for the injections of alcohol and whiskey. As the canulæ had been introduced while the animal was under ether in the morning, no anæsthetic was employed in making connection with the kymograph, and none was used until 3.31/30". The pulse rate varied during the first half-hour from 210 to 190, the respirations were about thirteen in the minute, except during periods of struggling, as when the stomach tube was introduced.

Time P. M.		Mean arterial pressure (carotid artery) in mm. Hg.	Remarks.
H. M. S.	H. M. S.		
3 08 00	to 3 08 45	132	
3 09 03	to 3 10 03	126	5 c. c. whiskey injected subcutaneously.
3 10 03	to 3 10 48	120	
3 16 53	to 3 17 53	129	
3 17 53	to 3 19 06	143	Rise of pressure due to introduction of stomach tube.
3 19 06	to 3 20 06	136	Injection of 15 c. c. whiskey into stomach.
3 20 06	to 3 21 06	134	
3 27 06	to 3 28 06	No rise of pressure.	
3 28 06	to 3 29 20	129	
3 29 20	to 3 29 55	133	Injection of 15 c. c. forty-five per cent. alcohol into the stomach.
3 29 55	to 3 30 27	138	Sudden and sharp but small rise of pressure at 3.29/15" in course of struggling.
3 30 27	to 3 31 30	127	

Time P. M.		Mean arterial pressure (carotid artery) in mm. Hg.	Remarks.
H. M. S.	H. M. S.		
3 31 30	to 4 58		Some ether given. Aconitine injected in small doses at wide intervals.
4 58 00	to 4 59 05	114 Pulse rate, 175 per minute.	
4 59 05	to 4 59 58	108 Pulse rate, 159.	Injection of 4 c. c. fifty per cent. alcohol into jugular vein.
4 59 58	to 4 60 58	109 Pulse rate, 144.	
4 60 58	to 4 61 35	106 Pulse rate, 138.	Respirations increasing in rapidity.
4 61 35	to 4 62 10	101 Pulse rate, 139.	Injection of 4 c. c. fifty per cent. alcohol into jugular vein.
4 62 10	to 4 62 50	Slight fall of pressure. Pulse more rapid.	Respirations more than doubled in frequency.
4 62 50		103 Pulse rate, 175.	
4 65 13		100	
4 65 13	to 4 65 22		0.005 grams digitalin injected into jugular vein.
4 65 47		142	Maximum pressure. Due entirely to the digitalin. Subsequently, pressure fell to 125, then to 110, then rose again to 120. No struggles.

In Experiment III. the conditions appeared to be favorable to the action of a circulatory stimulant. The animal had first been bled, yet alcohol, either pure or in the form of whiskey, was unable to raise the blood pressure when injected into the stomach. Even fifty per cent. solutions, thrown directly into a vein, were ineffective in this respect, though greatly increasing the pulse rate and the respiration. On account of the previous injection of aconitine, made for reasons which do not concern the present paper, no stress is to be laid upon this behavior of the pulse and respiration. It is to be noted, however, that while alcohol was ineffective here, as in the previous experiments in raising the arterial pressure, an injection of digitalin was

followed promptly by its characteristic effect, and there is no reason to doubt that any other circulatory stimulant would have been able to raise the arterial pressure.

The above experiments show that in dogs, at least, moderate quantities of alcohol or of alcoholic beverages have no appreciable direct influence on arterial pressure when disturbing local influences are eliminated. The dog and the human being react so similarly to circulatory stimulants as a class that it is only fair to assume that alcohol also would give results like those cited if its action on human beings could be tested with the help of the mercurial manometer.

We have seen that those experimenters who believe that alcohol in small quantities causes a rise of blood pressure claim to see additional proof for this opinion in the fact that when the spinal cord has been severed in its upper portion this agent is still able to raise the arterial pressure. Inasmuch as the vasomotor centre is here severed from all connection with the peripheral arteries, and since alcohol is demonstrably without influence on the cardio-inhibitory and accelerator apparatus and on the isolated arteries, any rise of pressure now observed is referred by these experimenters to the stimulating influence of alcohol upon the heart itself. It is difficult to understand how these writers reconcile this opinion with the results obtained by others in testing the action of alcohol on the isolated heart.

Those who have observed no rise of pressure in animals with an intact nervous system have not thought it worth while to test the action of alcohol on animals whose spinal cord has been severed. These investigators, among whom the writer wishes to be numbered, believe that alcohol does not directly stimulate either the heart or the vasomotor centres. An appeal to the cut-cord experiment is not decisive, because its results often contradict those obtained in experiments on the intact animal or on the isolated heart. It is generally assumed that a rise of pressure observed after the section of the cord as following the injection of a drug, which under other conditions has no stimulating action on the vasomotor medullary centres or on the heart, is due solely to a local stimulating action on the walls of the peripheral arteries. But this opinion is not always tenable. For, as we shall see, alcohol often causes a very noticeable rise in the arterial pressure in an animal whose cord has been severed,

and yet it is not able to constrict the "isolated" peripheral arteries. When the results obtained in cut-cord experiments, as in some of those which follow, are so directly opposed to those obtained in experiments on intact animals and on the "isolated" heart and "isolated" peripheral arteries, we can only assume that these contradicting results derive their character from an abnormal irritability of the heart, the peripheral arteries or the spinal vasomotor centres, or from a combination of these causes. A study of the behavior of the circulatory apparatus after section of the upper part of the cord shows that minor fluctuations of pressure are not uncommon, and that the rapid injection of small quantities of an indifferent solution (NaCl 0.75 per cent.) often causes as great a rise of pressure as small quantities of alcohol. If normal saline solutions have an abnormal action in cut-cord experiments, it need not be a matter of surprise that alcohol also acts in a remarkable manner.

The following protocols of cut-cord experiments are submitted in the belief that disturbing factors which it is impossible, in the absence of further experiments, to define clearly are responsible for the rise of pressure so frequently noted in their columns; in brief, that the results which are obtained in the state of shock incident to the severe operation of severing the cord cannot outweigh the many concordant results of experiments on isolated organs, on uninjured animals, or on such as have been subjected to minor operations only.

It is to be noted that alcoholic solutions of varying strength have been employed in the following as in the preceding experiments, and it is repeated that solutions stronger than ten per cent. by volume have been employed solely because earlier investigators have frequently made use of such, and not for the reason that they throw more light on the question as to how alcohol acts when absorbed into the blood from the digestive tract.

Cut-cord Experiment I. Male dog, full grown. Weight, 7070 grams. Spinal cord cut at 3.40 P M. between first and second cervical vertebræ. Artificial respiration. Alcohol allowed to flow from burette into right femoral vein.

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Time P. M.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.		H. M. S.	
3 35	154		
3 40	section of cord.		
4 20 31	68	108	
4 20 50	68	93 (4 20 56) (4 21 56)	
4 20 56	68		Ten per cent. alcohol flows into femoral vein.
		113 (4 21 56) (4 22 56)	
4 22 22	75		Alcohol cut off. 8.5 c. c. injected.
4 23 30	75		
		110 (4 24 30) (4 25 30)	
4 25 30	74		Ten per cent. alcohol again.
		109 (4 25 30) (4 26 30)	
4 27 50	61	109 (4 26 30) (4 27 30)	Alcohol cut off. 10.5 c. c. this time.
4 29 30	59	105 (4 27 30) (4 28 30)	
4 30	66	102 (4 29) (4 30)	Ten per cent. alcohol again.
4 30 25	72		Alcohol cut off. 10 c. c. this time.
		90 (4 30) (4 31)	
4 32 25	65		
		101 (4 32 15) (4 33 15)	
4 38	66		
4 41 30	66	103 (4 32 15) (4 33 15)	
4 42 20	65		
4 42 30	64		
4 43 54	64		
4 44 30	69		Twenty per cent. alcohol 6.3 c. c. forced in very rapidly. Causes sudden elevation of curve.
		102 (4 44 30) (4 45 30)	
4 44 36	76		Due to fast injection, very temporary rise.
4 44 46	68		
4 45 12	65		Twenty per cent. alcohol again.
4 45 42	68		Turned off. 5.2 c. c. in thirty seconds.

Time P. M.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.		H. M. S.	
4 48	63		
4 49 24	54		Twenty per cent. alcohol turned on.
4 50 16	64		Twenty per cent. alcohol turned off. 10 c. c. injected in five seconds.
4 52 15	59		
4 52 30	56		
4 53 30	58		
4 54	59		
4 54 30	59		
4 55 20	57		Twenty-five per cent. alcohol turned on.
4 55 45	59		Still flowing.
4 56	62		Still flowing.
4 56 30	68		Alcohol turned off. 10 c. c. in seventy seconds.
4 57	65		
4 57 30	62		
4 59 30		110 (4 59 30) (4 60 30)	
5 03 30	65		

Experiment II. Dog of medium size. Cord severed between first and second cervical vertebræ. Arterial pressure before cord was cut, 86 mm. Alcoholic solutions of varying strength injected into right femoral vein from burette as before. Artificial respiration.

Time P. M.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.		H. M. S.	
3 28 57	65	175 (3 28 57) (3 29 57)	
3 29 24	65		
3 30 10	64		
3 31 10	65		
3 32 10	68		
3 33 40	59		
3 34 10	67	165 (3 34 10) (3 35 10)	
3 37 40	60		
3 37 45			Forty per cent. alcohol turned on.
3 38 25	57		Still flowing.
3 38 50	59		Alcohol turned off. 8.8 c. c. in sixty-five seconds.

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Time P. M.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.		H. M. S.	
3 39 50	66		
3 40 40	62		Forty per cent. alcohol again.
3 41 20	80	134 (3 41 20)	Still flowing.
		(3 42 20)	
3 41 45	83		Still flowing.
3 42 20	80		Alcohol turned off. 10 c. c. in 100 seconds.
3 43	64	164 (3 43)	
		(3 44)	
3 43 30	66		
3 45	67	156 (3 45)	Forty per cent. alcohol again.
		(3 46)	
3 46	67		Forty per cent. alcohol turned off 4.4 c. c. in sixty seconds.
3 47	65	163 (3 47)	
		(3 48)	
3 49	67	161 (3 49)	Forty per cent. alcohol again.
		(3 50)	
3 49 36	76		Forty per cent. alcohol turned off. 5.3 c. c. in thirty-six seconds.
3 50 16	64		
3 51	64		
3 56	72	161 (3 55)	Forty per cent. alcohol again.
		(3 56)	
3 56 40	82	152 (3 56 20)	Forty per cent. alcohol turned off. 8 c. c. in forty seconds.
		(3 56 50)	
3 57 15	68		
3 57 45	73	158 (3 58)	Left sciatic nerve severed.
		(3 59)	
3 59 50	75		Began preparation of left saphenous nerve.
		159 (3 59 50)	
4 00 30	72	(4 00 50)	
4 01 10	72		
4 02	72		
4 02 34			Preparation of saphenous nerve completed.
4 02 44	64		
4 03 30	66		
4 03 46	66		Stimulated saphenous nerve with weak secondary current for fifteen seconds.
4 08 30	63		Ten per cent. alcohol turned on.

THE LIQUOR PROBLEM.

Time P. M.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.		H. M. S.	
4 10	66		Alcohol still flowing.
4 11	67		" " "
4 11 45	72		" " "
4 12 45	74		Alcohol turned off. 39.3 c. c. in four minutes fifteen seconds.
4 13 45	67		
		154 (4 20) (4 21)	
4 21	66		Twenty-five per cent. alcohol turned on.
4 22	64		Twenty-five per cent. alcohol still flowing.
		165 (4 21) (4 23)	
4 22 30	66		Twenty-five per cent. alcohol turned off. 26.7 c. c. in four minutes.
4 25	64	161 (4 25 10) (4 26 10)	
4 29 30	65		
4 31 20	72		
4 32 25	70		Forty per cent. alcohol turned on.
4 33 08	74		Forty per cent. alcohol turned off. 4 c. c. in forty-seven seconds.
4 39 08	72		
4 41 43	75		
4 42 26	70		Forty per cent. alcohol again.
4 42 50	74		Still flowing.
4 43 14	63		Alcohol turned off. 18.4 c. c. in forty-eight seconds.
4 44 10	20		Heart beats slowly and feebly.
4 44 53	14		
4 47 23	76		Heart has nearly recovered.
4 53	81	135	
4 57	77	138	Forty per cent. alcohol again.
4 57 15	79		Still flowing.
4 57 20	86	129 (4 57 20) (4 58 20)	Still flowing ; momentary rise of pressure.
4 58 20	72	126 (4 58 20) (4 59 20)	Alcohol turned off. 11.7 c. c. in eighty seconds.
4 59 20	71		
5 01 05	68	131	

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Time P. M.	Mean arterial pressure (carotid artery) in mm; Hg.	Pulse rate.	Remarks.
H. M. S.		H. M. S.	
5 02 05	69		Twenty-five per cent. alcohol turned on.
5 02 55	60		Twenty-five per cent. alcohol turned off. 18.6 c. c. in fifty seconds.
5 03 15	47		
5 03 55	32		
5 04 25	14		
5 06 25	28		
5 07 05	30		

Experiment III. Small bitch. Mean carotid pressure before section of cord, 100 mm. Cord completely severed at 3.34 P. M. Injections from burette into right femoral vein as before. Also into left femoral artery.

Time.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.			
3 34	39	100	
3 38 20	40		
3 39 26	40		Twenty-five per cent. alcohol turned on.
3 39 46	50		Twenty-five per cent. alcohol turned off. 7.6 c. c. in twenty seconds.
3 40 10	65	86	
3 40 50	50		
3 41 30	43	91	
3 42 15	40		Twenty-five per cent. alcohol again.
3 42 57	45	87	Still flowing.
3 43 22	48		Still flowing.
3 43 47	46		Turned off. 7 c. c. in sixty-seven seconds.
3 45 21	34	85	
3 47 47	34		Ten per cent. alcohol turned on.
3 48 47	48	86	Alcohol turned off 16.8 c. c. in sixty seconds.
3 49 47	42		
		86	
3 50 47	42		
3 53 11	44		Normal saline solution from burette.
		83	
3 54 02	52		Saline solution turned off. 24.3 c. c. in fifty-one seconds.
3 54 36			

Time.	Mean arterial pressure (carotid artery) in mm. Hg.	Pulse rate.	Remarks.
H. M. S.			
		84	
3 56 16	50		Injection ten per cent. alcohol into left femoral artery.
		85	
3 57 03	50		Ceased injection. 11.4 c. c. in forty-seven seconds.
3 57 17	50		
4 00 10	48		
4 02 12	48		Injected twenty-five per cent. alcohol into right femoral artery. 3.4 c. c. caused no change in the pressure.
4 03 12	52		
4 07 11	54		
4 07 17	54	80	Twenty-five per cent. alcohol allowed to flow into left femoral vein.
4 07 52	66		Ceased injection. 9 c. c. in thirty-five seconds.
4 08 02	66	78	
4 09 02	62	75	
4 10 02	60		
4 11 02	52		
4 12 02	49		
4 13 02	48		
4 15 22	43		Forced twenty-five per cent. alcohol into femoral artery.
4 16 04	43		Ceased injection. 4.5 c. c. in forty-two seconds.
4 16 16	44		
4 18 12	45		
4 20 12	48	77	
4 24 06	54		Injection forty per cent. alcohol into femoral vein.
4 24 36	69		Still flowing.
4 25 06	62		Still flowing.
4 24 25	50		Alcohol turned off. 13.6 c. c. in seventy-nine seconds.
4 25 35	42		
4 26 05	28		
4 26 45	24		
4 27 20	38		

Experiment IV. Male dog. Weight, 15,770 grams. Before section of the cord, arterial pressure varied from 97 to 105 mm. Considerable hemorrhage during operation. Cord

cut at 4.45. Injections by means of a syringe into the right jugular vein. Pressures calculated by Dr. A. C. Crawford.

Time.	Mean arterial pressure (left femoral artery) in mm. Hg.	Remarks.
H. M. S.		
4 45	25	
5 05	32	50 c. c. normal saline solution into the stomach.
5 12	34	Slow injection of 11 c. c. ten per cent. alcohol. No change of pressure.
5 16	32	Injection of 11 c. c. five per cent. alcohol.
5 21 30	29	Injection of 11 c. c. ten per cent. alcohol.
5 23		Injection of 11 c. c. ten per cent. alcohol.
5 23 30	29.4	" " " "
5 24 30	28.5	" " " "
5 26 15	28.5	" " " "
5 26 30	26	Injection of 11 c. e. twenty-five per cent. alcohol.
5 32	27	Injection of 11 c. c. twenty-five per cent. alcohol.

An examination of the protocols of the four preceding experiments shows that in only one of them (Experiment IV.) did alcohol fail to raise the arterial pressure. In Experiment IV. its only effect was to cause a steadily progressive, although slight, lowering of the pressure. In Experiment II. minor variations of from 3 to 8 mm. were observed before alcohol was injected. It will be noted that the injections, with now and then an exception, raised the arterial pressure to the extent of from 6 to 12 mm., and that once in Experiment II. an exceptionally large rise of 21 mm. was obtained. Solutions injected very quickly into a vein had a much more pronounced effect than when injected slowly. Quantities of twenty-five or forty per cent. solutions, which caused a noticeable rise of pressure when injected into a vein, were entirely devoid of action when thrown into an artery. In this case the alcohol would reach the heart in a more diluted state than when injected intravenously, the conditions being somewhat comparable to the passage of alcohol through the walls of the digestive tract.

Changes in the pulse rate were inconstant, although a slowing of the heart's rhythm often coincided with a rise of pressure. Any considerable quantity, say 18 to 25 c. c. of a twenty-five to forty per cent. solution, injected rapidly, will be

followed by a very decided lowering of the pressure and great enfeeblement of the heart.

It is not improbable that in the case of human beings alcoholics also have a similar slight but temporary stimulating action in conditions of not too profound shock or depression of the central nervous system. Beneficial effects apparently could be obtained only from the use of moderate quantities. Wood has shown, and the writer can substantiate his statement, that it is worse than useless to attempt to revive with alcohol an animal that has received an overdose of chloroform or ether in the course of an anæsthesia.

An explanation of the slight blood-pressure raising action of small quantities of alcohol, as shown in the majority of the cut-cord experiments above described, cannot be given without further experiments. In view of the previously described experiments on the isolated heart and vessels and on intact animals, it is fair to assume that this effect is to be ascribed to an anomalous condition of some part of the circulatory apparatus, rather than to a stimulating power inherent in alcohol. We have seen that in respect to the circulatory apparatus its usual action is that of an indirect stimulant only, and that in the case of the cut-cord experiment it is entirely devoid of stimulating power when the conditions are unfavorable, as in Experiment IV.

MANNER IN WHICH ALCOHOL LOWERS THE BLOOD PRESSURE.

We may now inquire briefly into the physiological mechanics by which the blood pressure is lowered by large quantities of alcohol.

It has already been stated that even in the early stage of the action of alcohol the vessels of the skin and of the brain are somewhat flushed, but that little if any lowering of the blood pressure is seen during this stage. It is only in a later stage, when the abdominal arteries are widely dilated, that a marked depression of the arterial pressure occurs.

There has been considerable discussion, not only as to the amount of this vascular dilation and the part it plays in causing the fall of pressure, but also as to the manner in which it is brought about.

The greater number of authorities in this field, however,

admit that the vascular dilation, which is so apparent after small doses of alcohol, increases with larger quantities until finally, as already stated, the abdominal vessels also become dilated. Assuming this to be the case, we must grant that this dilation can only be brought about either by a local paralyzing action of the alcohol on the walls of the vessels or on the peripheral terminations of the vasomotor nerves in the walls, or by an action on the circulatory centres of the medulla and cord, or by a combination of these actions.

Now it will be remembered that Kobert has shown that it is highly improbable that alcohol in moderate quantities has any direct dilating action on the walls of the vessels. Further, Gutnikow has lately demonstrated that alcohol in large amounts does not paralyze the peripheral terminations of the vasoconstrictor nerves situated in the walls of the arteries. We may, therefore, hold to the opinion that a local and depressant action of alcohol on the periphery of the vascular apparatus is only likely to be seen when enormous doses of alcohol are introduced.

Gutnikow has, however, demonstrated that the vasoconstrictor centres of the medulla do not escape the depressant action of the alcohol; that their reflex excitability is decidedly lowered when fairly large quantities of alcohol are administered.

He has shown that the asphyxiation of an animal that has received alcohol does not in the great majority of cases cause a rise of blood pressure, such as may always be seen in animals that have received no alcohol. He has also shown that strychnine given to alcoholized animals falls far short of its usual effect in raising the blood pressure. These results point to a depressed state of the vasoconstrictor centre in the animals that had received alcohol.

But as some might raise objections to the conclusiveness of the proof thus far advanced, Gutnikow took the pains to compare both the direct and the indirect excitability of the vasomotor centres in the medulla before and after alcohol. His experiments show that these centres were less able to respond after alcohol, not only to a direct application of an electrical stimulus to the medulla, but also to the stimulation of the sciatic nerve.

At this very time, however, when the vasoconstrictor centres

were in a state of depression, it was found by Gutnikow that the peripheral terminations of the vasoconstrictor nerves were in nowise depressed; for stimulation of the divided splanchnic nerves caused the blood pressure to rise to about the same height as before the administration of alcohol.

It is an accepted fact of physiology that a depressed condition of the vasoconstrictor centres is followed by a dilatation of the peripheral vessels.

We must believe, in view of the experiments cited, that alcohol, like its pharmacological congeners, chloroform, paraldehyde, etc., acts powerfully on the nervous centres which control the calibre of the vessels, and that it dilates these by a depressant action on the nerve centres.

But this depressant action on the nerve centres is only demonstrable when *large* quantities of alcohol are administered. How, then, are we to explain the primary flushing of the face and other parts of the body which is seen after moderate quantities of alcohol? It is evident from all that has been said that here too we can only find the explanation in some action of the alcohol in the central nervous system. When small doses are employed it is impossible to show that the vasomotor centres are depressed. The same difficulty is encountered as Durdafi has recently shown in explaining the vasodilation of amyl nitrite and nitroglycerine. This writer concludes from his experiments that these drugs neither depress the vasoconstrictor centres nor stimulate the vasodilator centres at a time when they cause considerable vascular dilation. To explain the action of the two drugs he is obliged to fall back on the hypothesis that they annul the effect of the normal stimulus, whose action on the opposing nerve centres of the circulation is to maintain a normal blood pressure and an average calibre of the vessels. To the absence of this normal or physiological stimulus he ascribes the effects of amyl nitrite, such as the dilated vessels and the lowered blood pressure.

We must admit, then, that we have only hypotheses and not facts to offer in explanation of the primary flushing of the skin after small quantities of alcohol. The usual assumption is that it is brought about by a slight depressant action of the alcohol on the vasoconstrictor centres, which, however, is not great enough to lower their excitability in response to experimental

tests. The cause must be sought in the nerve apparatus which controls the calibre of the vessels, since we have seen alcohol does not easily affect the muscles of the wall or the nerve terminals.

In view of the work of Martin and others we must also assume that when the blood pressure has fallen to a low level, as in cases of very deep intoxication, a weakening of the heart's action occurs, and that this is in some degree responsible for the low blood pressure.

BRIEF SUMMARY OF THE ACTION OF ALCOHOL ON THE VASCULAR APPARATUS.

So far as present experimental evidence goes, we may say —

1. That alcohol as such, that is, when it is introduced into the circulation with the avoidance of local irritation, is not a circulatory "stimulant."

2. Alcohol in moderate quantities, say a pint of wine, has no direct action on the heart itself, either in the way of stimulating or depressing it. This statement is based on the results of laboratory experiments, extending over short periods of time only, and does not imply that it holds for the steady daily use of alcohol in this quantity. Large quantities of alcohol weaken the heart in the manner already described.

It has also no action either on the peripheral or central ends of the nerves which control the rate and force of the heart, except probably in unusual circumstances, such as prolonged and severe intoxication.

3. Alcohol in moderate quantities has also no direct action on the walls of the blood vessels, either on their muscular portions or on the peripheral terminations of their vasomotor nerves. This statement also refers only to the results of single administrations. For the pathological effects of the continued use of "moderate" quantities the writings of pathologists must be consulted.

4. In moderate quantities it has also no appreciable effect on the arterial blood pressure. When a change in this becomes apparent it is always in the direction of a fall and not of a rise. An exception is seen when the spinal cord is severed in its upper portion. In this case a small and temporary rise of pressure follows the rapid injection of diluted alcohol, except in those

instances when the blood pressure is very low, say 30 mm. or below. It is assumed that an anomalous condition of some part of the circulatory apparatus accounts for this unusual effect. In the early stages of its action it usually causes some degree of flushing of the skin and brain, and later, when very large quantities have been taken, vascular dilatation of the abdominal vessels occurs. The fall of blood pressure due to very large quantities is a toxic phenomenon and is never met with under ordinary circumstances. It is due to the depressant action of the alcohol on the nervous centres which control the calibres of the arteries and also in part to the weakened heart.

5. It is not to be inferred that the above statements forbid a reasonable and prudent use of alcohol to therapeutics. The day is happily past when the therapist plied his patient with a number of bottles of wine a day in the belief that he could stimulate the heart, lower the temperature, supply nutriment, and effect other good ends without detriment of any kind, by giving these large quantities. This broad question of the therapeutic use of wine cannot be entered on in detail at this point. It may be remarked, however, that the cerebral effects of alcohol, its numerous indirect influences, its action in causing a different balance in the parts and functions of the vascular apparatus, often justify its moderate use in therapeutics.

6. Alcohol, by virtue of its local action on mucous membranes, and also by virtue of its cerebral action, is capable of affecting the several parts of the vascular apparatus in a number of ways, the resulting effects often being such that the term "circulatory stimulant" is often applicable. Such indirect effects, which are shown by all of the pharmacological congeners of alcohol, are familiar in the use of alcohol in daily life and in medical practice.

Of these indirect effects none is more often observed than a quickening or slowing in the pulse rate, as is frequently seen in medical practice. These indirect influences must not be allowed to hide the true character of alcohol, which is always depressant in kind, and which easily gets the upper hand of the effects just noted. In a word, alcohol, in respect to its inherent action, when once in the blood and tissues, must be classed with the anæsthetics and narcotics.

III. THE ACTION OF ALCOHOL ON THE RESPIRATION.

In studying the influence of alcohol on the respiration, we encounter difficulties similar to those found in its action on the vascular apparatus.

Of all the automatic centres none is more easily influenced by psychical conditions, by afferent impulses arising in various organs, and by pharmacological agents, than the respiratory centre. Not only is it easily influenced by the direct action of poisons circulating in the blood, but still more by stimuli which have their origin in the peripheral parts of the body.

Since alcoholic beverages have as a class a stimulating action on the digestive tract, and easily induce slight changes in the vascular apparatus and in the emotional state, it is natural to suppose that they will not be without action on the respiratory function. Indeed, it is a belief deeply rooted in the popular mind that certain alcoholic beverages, such as brandy and good wine, are true respiratory stimulants, and this belief is also held by the majority of physicians. When we inquire into the meaning of this term we find that investigators apply it to such agents as cause an increase in the volume of air passing into the lungs in a given time, provided that this result is attained without incoördination of thoracic, diaphragmatic, or abdominal movements. It is evident from what has been said that such a result may follow in consequence of the direct action of an agent upon the cells of the respiratory centre, or as a remote or reflex effect of local action in the digestive tract, or of altered psychical states, or of changes in the metabolic processes which incite the tissues to make a larger demand for oxygen, or even, as Richet has pointed out, as a consequence of reflex action directed toward regulating the body temperature by a larger exhalation of water vapor.

When a given substance acts in the first of these ways it is called a primary or specific respiratory stimulant, and it may be remarked that there are but few in this class, one of its best examples being carbonic acid, which causes an increase both in the number and in the depth of the individual respirations. Direct depressants of the respiratory centre are, however, very numerous. Chloroform and opium are examples of this class.

Substances that only affect the respiratory centre by first

causing some alteration elsewhere in the body are called indirect stimulants or depressants, as the case may be. By far the greater number of respiratory stimulants belong to this class of indirect stimulants.

In experiments made to determine whether a given substance is a respiratory stimulant or depressant, it is fallacious to rely merely on the number of respirations that take place in a given time. The number of respirations may be greater than usual and yet the amount of air that passes through the lungs may be less than in the normal period, because the individual respirations are shallower. On the other hand, the number of respirations in a given period may be smaller, and yet each respiratory movement may be so much deeper that more air passes into the lungs than in the normal period.

Until quite recently too much stress was laid on mere counts of the respirations and on the excursions of the levers of tambours, etc., attached to the chest, abdominal wall, or diaphragm; in other words, to the results obtained by the graphic method. The data obtained in this way, in experiments on both men and animals, have been conflicting and contradictory. This method is of far greater value when combined with the gasometric or air-measurement method than when used by itself. Its greatest value in such studies as we are about to describe lies in the fact that it serves to detect an inharmonious working of the individual parts of the respiratory apparatus. In the gasometric method we endeavor to measure the amount that passes into or out of the lungs during each respiratory act, by means of a delicate air meter or by some method of fluid displacement in which all opposition to the act of breathing is reduced to a minimum. Sometimes, too, the measurement of the amount of oxygen absorbed by the blood during each inspiration is made the basis of comparison, but in this case other phases of the problem are kept in view.

Before the middle of the present century a number of investigators studied the influence of alcohol on metabolism by measuring the amount of carbonic acid exhaled. While it is not the object of the present paper to discuss this point, it may be well to refer to some of these early researches, since their authors frequently note the influence of alcohol on the number of the respirations, and in a few of them the amount of air

taken into the lungs under the influence of alcohol was also measured. Thus, the treatise of K. Vierordt on the physiology of the respiration (1845) contains a number of experiments illustrating the action of alcohol on the rate of respiration and on the excretion of carbonic acid. I have taken at random two of his experiments made on himself :

June 10. H. M.	Respirations.	Pulse.	CO ₂ in 100 parts of air (in c. c.).	Volume of air expired in one respiration (in c. c.).
5 40	11	69	4.40	
5 50 to } 6 10 }	3 glasses of fairly strong beer were taken.			
6 17	10	86	4.45	
August 5. H. M.				
10 11	12	66	4.63	515
10 15 to } 10 35 }	one bottle of light white wine taken.			
10 49	12	75	4.13	516

It will be seen that in Vierordt's case there was no indication of any stimulation of the respiration as a consequence of having taken beer or wine.

The investigations of Prout, Berzelius, and Böcker also belong to this early period, but need not be reviewed here because we are less concerned with the influence of alcohol on gaseous exchange, a phase of the question which chiefly interested them, and also because modern investigations surpass them in the excellence of their experimental method.

E. Smith (1859), whose investigations belong to the class just cited, makes the following statements as to the influence of various alcoholics on the respiratory rate: "The rate of the respiration was in almost all instances lessened in both of us, whilst that of pulsation was as constantly increased in myself, but not in Mr. Moul."

In Zimmerberg's experiments (1869) on dogs no effect was discovered other than a gradual slowing of the respiratory rate as the amount of alcohol injected into the stomach was increased. In the case of rabbits, also, 10 to 20 c. c. of thirty per cent. alcohol had a retarding action.

An interesting paper which appeared at this time (1869) is the dissertation of Berg on the influence of the respiratory rate and depth on the output of carbonic acid from the lungs.

This author also studied in himself the effects of ethyl alcohol on the respiration. Later experimenters have criticised him for taking a cup of black coffee before beginning his experiments and for adding ethereal oils and sugar to his solution of alcohol. It may be noted also that the alcohol had an unpleasant action on Berg; he complains that he suffered from nausea and headache after taking it.

Two of Berg's summaries as given in the following tables will suffice to show what his results were. The tests were begun at 9 A. M. and were repeated at intervals until 3 P. M. After one or two o'clock he usually suffered from nausea and headache. The considerable quantity of six ounces of alcohol of 58° strength (Tralles) was taken in seven portions in the short space of half an hour, between 7.30 and 8.00 A. M. As already stated, a little sugar and a small quantity of several ethereal oils were added to increase its palatability, and a piece of bread and butter was eaten at the same time.

Experiment I.

Respirations of varying frequency and of arbitrary depth.

	Pulse in one minute.	Volume of air (in litres) passing out every fifteen minutes.	Volume of air (in c. c.) in a single respiration.	CO ₂ of one litre of air in grams.	CO ₂ (in grams) in air expired in fifteen minutes.	CO ₂ (in grams) in air of one expiration.	CO ₂ (in volume per cent.) in 100 c. c. of expired air.
After alcohol	59.7	103.20	483	0.0672	6.901	0.0331	3.40
Without alcohol	56.0	89.47	419	0.0672	5.964	0.0339	3.40
Difference	+3.7	+13.73	+64	0.0	+0.937	0.0008	0.0

Experiment II.

Frequency and depth of the respirations at natural rate.

	Respiratory rate.	Pulse in one minute.	Volume of air (in litres) expired in fifteen minutes.	Volume (in c. c.) in one respiration.	CO ₂ (in grams) in one litre of air.	CO ₂ (in grams) in air expired in fifteen minutes.	CO ₂ in air of one respiration.	CO ₂ (in volume per cent.) in 100 c. c. of expired air.
After alcohol	10.6	61.4	72.66	461	0.0769	5.630	0.0356	3.82
Without alcohol	9.9	57.8	50.88	345	0.0804	4.108	0.0273	4.08
Difference	+0.7	+3.6	+21.78	+116	-0.0035	+1.522	+0.0083	-0.26

Leaving out of consideration here the question as to how the carbonic acid output is affected by alcohol, it is evident that Berg finds alcohol to be a rapidly acting stimulant, and that it increases both the rate of the respiration and also the volume of air which passes through the lungs in each individual respiration. Berg admits that a certain share in this effect must be attributed to the small quantity of ethereal oil and sugar present in the alcohol taken by him.

Marvaud (1872) also claims that the respirations become more frequent under the influence of alcohol, but with an increase in the dose they become less frequent and feeble. He cites the experiment of Lallemand and Perrin, who observed that a horse which had received a large quantity of alcohol had only five respirations in the minute during a period of about a quarter of an hour. Marvaud's own experiments were made on rabbits, and he offers graphic tracings obtained with the apparatus of Marey in support of his opinion that the respiration is first stimulated and then depressed by alcohol.

Dogiel (1874) finds that small quantities of alcohol injected directly into the jugular vein or into the stomach cause in dogs an increase in the respiratory rate, while large quantities cause a decrease, the individual respirations becoming shallower as they become more infrequent. According to this investigator, alcohol in small doses is a respiratory stimulant.

Parkes (1870-74), in his numerous experiments on the effects of alcoholic stimulants on soldiers, paid special attention to the respiration. In studying the effect of "dietetic doses" of

brandy the respirations were taken in twenty-three daily observations, and a table of mean values was constructed. Parkes arrived at the conclusion that the "respirations were not increased by brandy, but were rather lessened and were deeper in some of the experiments, the effect not being very marked." The use of claret did not enable him to trace any effect on the number or depth of the respirations.

To this period belong also the experiments of v. Boeck and Bauer (1874) on the influence of alcohol on the oxygen intake and the carbonic acid output. To cite the results of one of their experiments, 40 c. c. of thirty per cent. alcohol caused the carbonic acid output to increase thirty-five per cent. and the oxygen intake thirty-three per cent. This amount of a rather too concentrated alcohol induced gastro-intestinal disturbances in the dog used in the experiment, and also muscular movements, and to the latter the above increase in the respiratory interchange is attributed by the authors themselves. They question whether an increase of this sort ever occurs in man. Later experimenters have found so much to criticise in this investigation that further attention need not be given to it.

The investigation of Vogelius may be dismissed with a few words, although this writer used one of the best forms of respiration apparatus then known, Ludwig's modification of the apparatus of Regnault. In this form of apparatus the animal was made to breathe pure oxygen instead of air. Vogelius used rabbits, and states that the administration of alcohol caused a marked increase in the respiratory rate of these animals, a fact which all subsequent observers have substantiated. His statement that small quantities of alcohol cause an increase in the oxygen intake is substantiated by the recent experiments of Singer, as we shall see later. Larger quantities are declared to decrease the oxygen intake. This part of the work of Vogelius stands sharply contradicted by the late researches of Singer, to which reference will presently be made. Small quantities of absolute alcohol (5 to 15 c. c.) caused it to increase from sixteen to sixty-nine per cent.

The work of Wolfers which follows next in order is open to serious criticisms. In the first place, that sensitive and unreliable animal, the rabbit, was subjected to various operative proceedings which could not but vitiate the results obtained. A

canula having been inserted into the jugular vein, the animals were tied to a board and immersed in a warm bath. In many of the experiments the respiratory rate was but little changed by a few cubic centimetres of ten per cent. alcohol; repeated injections into the jugular vein of 3 or 5 c. c. of alcohol of this strength sometimes caused a slight increase, sometimes a slight fall, and then again very decided alterations in the rate.

Füth (1885) avoids some of the errors just alluded to. He notes that it is unallowable to use animals that have been operated upon in experiments such as we are now considering, and that the respiration is easily affected by a variety of influences. According to Füth, small doses of alcohol cause a lessening in the consumption of oxygen, and in the excretion of carbon dioxide, while large doses have a greater effect in this direction. On the average, a dose of 2.5 c. c. alcohol per kilogram of body weight diminishes the oxygen consumption of dogs and rabbits by about thirteen per cent. and the carbon dioxide by about eleven per cent.

Bodländer (1886), who directed the work of Füth, published similar experiments and at greater length. His results were the same. Both investigators interpret their results as signifying that alcohol spares other foods since it diminishes the consumption of oxygen. Although these researches do not appear to have any connection with our problem, we shall see presently that the influence of alcohol on the consumption of oxygen is, in the opinion of a recent investigator, one of prime importance in the explanation of its action on the respiratory movements.

We now approach a period of great improvement in the experimental methods. Zuntz, Geppert, Dreser, and their pupils have invented better ways of measuring the air passing through the lungs, and they have introduced experimental precautions which have led to a greater unanimity of opinion.

Zuntz and Berdez (1887) have made a series of experiments in which the latter breathed through a carefully fitted mouth-piece which was connected with a tube containing easily moved valves, the valves for the outgoing air being connected with a sensitive air meter. Only small or dietetic doses of alcohol were taken by Berdez, as somewhat larger quantities induced restlessness and tended to vitiate the experiment. Examina-

tion of the expired air not only showed how large a volume passed through the lungs, but also how much oxygen was consumed and how much carbonic acid was eliminated in the unit of time. The results obtained showed that small quantities of alcohol increased the total volume of air passing through the lungs by about nine per cent., oxygen absorption being increased by 3.5 per cent. and the carbonic acid outflow by 4.5 per cent. According to these investigators, therefore, alcohol is a respiratory stimulant, though one of only moderate power.

At this time also Geppert, at the suggestion of his teacher Binz, studied the effect of alcohol on the gas interchange of human beings. The ingenious apparatus employed was that of Zuntz and was so modified as to be adapted to the human body. The inspired and expired air were separately measured and analyzed and disturbing factors, such as arise in experiments on animals, were as much as possible eliminated. Four men varying in age from twenty-four to thirty-two years served as the subjects of the experiments, and moderate as well as larger quantities of ethyl alcohol, port wine, cognac, and Rhine wines (30 to 190 c. c. ethyl alcohol) were employed. The following tables, taken from the paper read by Professor Binz at a meeting of German physicians held at Wiesbaden in 1888, at which the whole question of the therapeutic value of alcohol was discussed, well illustrate Geppert's results.

RESPIRATION VOLUME MEASURED IN LITERS FOR PERIODS OF TEN MINUTES.

Before alcohol.	Immediately after the alcoholic beverage.	In succeeding periods.	Percentage of increase in the respiration volume calculated from the second column.
57	62	59	+8.7
61	57	55	-6.7
55	60	56	+9.0
54	57.5	52	+6.5
55	60	57	+9.0
45	49	-	+9.0
53	56	51	+6.0
54	59	53	+9.0
51	59	57	+15.

In commenting on this table Binz remarks that the results show an increase in the air intake and output of about seven per cent. The marked increase of fifteen per cent. in the last experiment was obtained with a German champagne, and in this

case the stimulation held on for a longer time than with the other beverages. It must be confessed, says Binz, that all this does not amount to much, but it nevertheless proves that alcohol and alcoholic beverages exert a clearly marked, though slight stimulating, action on the respiration of healthy human beings. In later researches of Binz's pupils, in which animals were employed, this statement is repeatedly emphasized, and especial stress is laid on the point that sound wines of a high flavor, that is, such as contain volatile esters and aldehydes in largest amounts, are more stimulating to the respiration than the plainer kinds.

Binz also remarks that in certain forms of illness a greater effect is probably produced than in the experiments cited, just as the temperature lowering action of the antipyretics is best seen in cases of fever, while in normal individuals little or no temperature lowering action can be observed.

In the present state of the question, then, we may say that experiments made by methods just described show that alcoholic beverages stimulate the respiration of human beings for a brief period immediately following their consumption. This stimulating effect is seen in a slight increase in the volume of air passing through the lungs, seven to nine per cent. of increase for ethyl alcohol, cognac, and plain wines, and possibly fifteen per cent. for foaming wines.

In this connection it will be of interest to describe the clinical experiments of v. Jaksch on the effect of alcohol on the respiration of children. This clinician, a man of wide experience in medicine, read his paper at the meeting of physicians at Wiesbaden already referred to. He belongs to that large majority who hold that alcoholics are stimulants of more or less power for the circulation and respiration. His paper shows that eleven children, each of whom received 20 c. c. of wine, or the equivalent of 1.3 grams of alcohol, reacted as follows a half hour after its administration. In five instances the respiratory rate was increased, in five no alteration in the rate was observed, and in one case the respirations were slowed. After the administration of 8 c. c. of cognac, or the equivalent of 3.2 grams of alcohol, the results in ten cases were as follows. In four of the children the respiratory rate was increased, in two it remained unaltered, and in four it was decreased.

After taking 3.2 grams of properly diluted ethyl alcohol, seven of the children showed an increase in the respiratory rate, four showed no change, and one a decrease.

The changes noted were not great, and it must be borne in mind that the method used was that of direct observation of the movements of the chest and of simple counting. It is highly probable that if the aero-metric method had been employed the results would have been like those which have since been obtained by the use of this method in the case of adults.

When we recall our definition of a respiratory stimulant as given at the beginning of this section, it is at once seen that mere counts of the respiration, even when these are coupled with close observation of the movements of the chest and abdomen, cannot settle the point as to whether a given agent is truly a respiratory stimulant.

In reply to the criticism of Bunge, that there must be some flaw in the work of Binz and his pupils, since alcohol belongs, pharmacologically speaking, to the depressants of the central nervous system and is therefore not likely to have any stimulating action of importance, Binz induced his pupil Heinz, and later Weissenfeld, Wendelstadt, and others, to take up this question again. Heinz made use of rabbits and measured the volume of air passing through the lungs in a given time under the influence of alcohol, paying no attention to the absorption of oxygen or the excretion of carbon dioxide. His experiments amply prove that, in this animal at least, alcohol decidedly increases both the frequency and the depth of the respirations. Thus, if the volume of air passing out of the lungs of a rabbit in twenty seconds is 179.75 c. c., the intravenous injection of a little very weak alcohol will immediately cause an increase to 204.25 c. c. in an equal period, and after a second injection the volume of air expired will even reach 330 c. c.

Binz himself repeated the experiments of Heinz, with the result of obtaining a maximum increase of ninety per cent. in the respiration volume during the forty minutes immediately following the intravenous injection of dilute alcohol. Even after subcutaneous injection he observed an increase of sixty-nine per cent.

Cerna (1893) has conducted experiments on dogs in which he finds "that alcohol in sufficient amounts not only produces

a decreased rate but also a diminution in the depth of the respiratory movements, this giving rise to a lower quantity of air passing in and out of the lungs than in the normal condition." He remarks that small doses do not markedly affect the respiratory rate, although sometimes causing an increase. His method, like most of those just described, involved tracheotomy and fitting a canula into a vein. "Two Müller valves were connected, by means of a rubber tubing and a Y-shaped glass tube, with the trachea of the animal experimented upon; and in turn, one of the bottles was left in contact with the external atmosphere, the other with large rubber bags, these again being made to communicate with a common air meter. Thus the air inspired by the animal was wholly transferred to the rubber bags, and the amount of air passing through the lungs in a certain period of time was more or less accurately ascertained by the meter. "I first measured the air for two or three periods of five minutes' duration each before injecting the drug and then proceeded to repeat the operation while the animal was under the influence of the alcohol."

The author then gives the protocols of four experiments. In three of these quantities of "pure alcohol" varying from 1 to 10 c. c. were injected, and in the fourth 215 c. c. of alcohol in twenty-five per cent. solution were continuously injected in the course of four periods, or twenty minutes. The dog used in this experiment weighed only 9.8 kilos and died suddenly at the end of the third period, fifteen minutes after the cessation of the injection. This experiment merely illustrates the action of an excessive quantity rapidly injected.

In criticism of the first three experiments it may be remarked that the injection into a vein of a small quantity of absolute or "pure alcohol" is not equivalent to the injection of the same quantity in dilute form, say in ten per cent. solution. In the former case the possibility of violent irritation of the veins at the point of injection, as also the formation of minute clots of coagulated albumen at the moment of the first contact of the strong alcohol and the blood, must be borne in mind. In fact the protocol of the third experiment reports the animal as dead at the close of the second period, after an injection of 10 c. c. of alcohol. This animal weighed 18.1 kilos and had received in all only 18 c. c. of "pure" alcohol, while Cerna's

own experiments lead him to believe that it requires as much as 38.5 c. c. of a twenty per cent. solution, per kilo of body weight when injected intravenously, to produce death, or more than 7 c. c. per kilo in terms of absolute alcohol administered in diluted forms. It is evident, therefore, that no inferences which bear on our subject can be drawn from these experiments.

The next experimenter who took up this subject and studied it with great care is Jaquet (1896). Like Binz, this author also makes use of rabbits. He agrees with Binz that small amounts of diluted alcohol cause the animal to breathe more air in the unit of time. There is therefore no lack of agreement between them as to the observed facts. But while the former arrives at the conclusion that alcohol is a true stimulant for the respiratory centre, the latter attributes to it no power of this sort, but declares it to be an indirect respiratory stimulant, acting only by virtue of its irritation in the stomach or elsewhere.

Jaquet uses the aero-metric method, only instead of measuring the exhaled air with an air meter he uses the simple and accurate method devised by Dreser, which is based upon the principle of displacing a measured volume of water without offering any but the most trifling resistance to the respiratory act. He does not tracheotomize his animals, but applies a well fitting mouthpiece which is connected with the measuring apparatus. He finds that alcoholic solutions of the strength employed by Binz cause the mucous membrane of the stomach of the rabbit to take on a bright rose-red color, that is, there is a local hyperæmia as a sign of irritation. An aqueous extract of mustard flour just strong enough to give a slight biting taste of oil of mustard to the tongue has a stimulating action on the respiration equal to that of a twenty-five per cent. solution of alcohol. Such a solution also causes an equal reddening of the gastric mucous membrane.

Again, after administering small doses of morphine just large enough, as Jaquet supposed, to lower somewhat the effects of a peripheral sensory irritation, but not large enough to depress the excitability of the respiratory centre, alcohol in the strength used was found to be inoperative as a stimulant. A true, centrally acting respiratory stimulant like hydrocyanic acid in small doses is, however, still active under these conditions.

On such grounds Jaquet asserts that alcohol is not a true stimulant for the respiratory centre, that it can only induce an increased activity on the part of this centre by local irritation of some more peripheral part of the body, and that its own direct action on this centre, as on other parts of the central nervous system, is of a depressant nature only. According to him all forms of alcoholic administration, whether by injection beneath the skin, into the stomach, or into a vein, or when taken into the lungs in the vaporized form, lead to this indirect stimulation of the respiratory centre. For example, experiments are given which show that when a rabbit is made to inhale the vapor of alcohol in sufficient concentration there occurs a marked increase in the respiration volume. After section of the pneumogastric nerves, which makes the transmission of sensory impulses from the irritated nerve terminals in the bronchial walls impossible, this result is no longer obtained.

Binz and his followers soon returned to the charge and met each of Jaquet's statements and experiments with counter-statements and experiments on rabbits. Under the leadership of Binz, Willmanns submitted each of Jaquet's conclusions to a critical experimental examination. He declares that Jaquet is wrong in thinking that gastric or other irritation is the cause of the observed increase in the respiratory activity. For this increase is still very large when ten per cent. solutions of alcohol are employed, solutions so weak, says Willmanns, that they do not cause hyperæmia in the gastric mucosa. He gives the details of experiments to prove that the injection into the stomach of solutions of mustard oil causes no increase at all in the respiratory activity, even when these solutions are so strong as to be more irritating than twenty per cent. alcohol.

Administration of alcohol in the form of vapor still increases the respiration volume, even when the pneumogastric nerves have been severed. Here, too, we meet with a direct contradiction of Jaquet's results. This increase is thought to be due to the stimulation of the respiratory centre by the alcohol so rapidly taken up by the blood in sufficient amounts and carried to this centre.

The quantity of morphine employed by Jaquet to lower the sensitiveness of the respiratory centre to impulses from the

lungs is declared by Willmanns to have been large enough to lower also the sensitiveness of this centre to direct stimulation, and that even after the use of morphine the intravenous injection of dilute alcohol is able to arouse this centre to increased activity. Lastly, says he, no deductions can be drawn from a comparison of the action of a powerful convulsant poison like hydrocyanic acid on the morphinized respiratory centre and that of alcohol in the like circumstances in such rational doses as were employed by Binz and his pupils. He also corroborates the experiments of Zuntz, Geppert, and Berdez, who, it will be remembered, attributed a stimulating action on the respiration to alcohol used in small quantities by human beings. In this work Geppert's modification of the apparatus of Zuntz was used, and two young students served as subjects. In both cases sherry wine in varying doses was employed, and a decided increase in the volume of air passing through the lungs was noted in each instance; an increase still noticeable two hours after the wine had been taken.

In a word, Willmann's experiments lead him to believe that alcohol is a true stimulant for the respiratory centre and does not act, as Jaquet believes, by virtue of local stimulation. As we shall see presently, the recent work of Singer furnishes us with a more plausible explanation of the action of alcohol than any that has yet been offered. Before taking up this work, however, we must give an outline of four other researches that have emanated from the laboratory of Binz, in which the power of alcohol and the volatile constituents of wines, cognac, etc., as respiratory stimulants is again insisted upon.

Two of these researches, those of Krautweg (1893) and Vogel (1897), on the action of the volatile constituents of alcoholic beverages, have already been referred to in the section on toxicity, and it will only be necessary to say here that the application of the aero-metric method shows that these constituents are somewhat more powerful as respiratory stimulants, both in animals and in men, than ethyl alcohol. The observations of medical men, that highly flavored wines are better respiratory stimulants than the plainer sorts, find support and explanation in these researches.

Weissenfeld (1898), who experimented on himself with a thirty-year-old Greek wine containing 13.7 per cent. alcohol

and with specially prepared malt wine, and who used a very sensitive air meter in measuring the volume of his expirations, finds himself in full agreement with Binz. Moderate doses (50 to 75 c. c.) of the Greek wine also raised the arterial pressure as measured with the sphygmomanometer of v. Basch. The difficulties and uncertainties attaching to this instrument are well appreciated by the author, for he quotes with approval the remark of Bozidar, that daily practice in its use for about three months is necessary before any work with it can be looked upon as at all trustworthy.

A single protocol will suffice to show the character of Weisenfeld's results.

Experiment VI.

		Average respiration volume per half minute.	Arterial pressure (radial artery).
Before wine	9 A. M.	3.10 litres.	130 m. m.
After 50 c. c. Greek wine.	9.15	3.46 "	145 "
	9.40	3.86 "	160 "
	10.20	3.36 "	150 "
	10.50	3.35 "	150 "

Other experiments are given to prove that the increase of respiratory volume is noticeable even when the wine has induced sleep; that a period of lessened respiratory activity does not succeed that of increased activity, at least not within the space of four hours after the administration of the wine; and that the increase in the blood pressure and in the respiratory activity is much greater when the body is weakened as the result of under-nutrition.

Far more extensive are the recent experiments of Wendelstadt. This investigator has measured the effects of pure alcohol, of cognac, and of various wines on a number of persons and has made it a prime object to test their action in conditions of bodily weariness. He has tabulated his results as well as those of his predecessors who have made use of trustworthy methods, and it is hoped that the presentation of his tables will give a better idea of the results obtained than a mere verbal statement could do. In all the experiments in which pure alcohol was used sugar and lemon juice were added to render it

palatable. The amount of sugar added was usually 12 grams, at least when the doses of alcohol approximated 20 c. c.

I.

Subject.	Ethyl alcohol given in c. c.	Percentage gain or loss in the re- spiration volume.
VIII.	5	+0.45
VIII.	15	+1.17
II.	15	+9.09
II.	15	+9.57
I.	15	+9.84
VI.	15	-11.02
VI.	15	-7.75
VII.	20	+6.39
V.	20	+2.89
IV.	20	+8.62
V.	25	+7.29
V.	40	+12.16
V.	60	+4.78

II. Effect of Wines.

Subject.	Amount of alcohol in the wines given (in cubic centimetres).	Kind of wine.	Percentage gain or loss in the respira- tion volume.
II.	4.25	Sherry	+7.70
I.	4.25	"	+9.14
II.	8.50	"	+7.71
I.	8.50	"	+3.09
V.	11.50	Rhine wine	+6.74
II.	12.75	Sherry	+14.61
VIII.	17	"	+9.80
V.	17	"	-7.58
II.	17	"	+9.82
I.	17	"	+7.83
IV.	25	"	+48.34
III.	40	Champagne	+14.14
V.	51	Sherry	+49.24
V.	60	Cognac	+24.01

III. Effect of ethyl alcohol and wine on persons exhausted by labor or exercise.

Subject.	Amount of alcohol given in c. c.	Percentage gain or loss in the respira- tion volume.
VIII.	5	+23.11
V.	10	+54.17
VI.	15	+25.75
V.	20	+12.09
IV.	20	+77.09
IV.	20	+50.46
VII.	20	+52.34
V.	60	+92.26
V.	17 in form of sherry	+83.60
V.	18 in form of cognac	+96.82

Wendelstadt has also tabulated the results of his predecessors in forms corresponding to his own as given below.

IV. Effect of ethyl alcohol on non-fatigued persons.

Person.	Amount of alco- hol in c. c.	Percentage gain or loss in the respira- tion volume.
Zuntz B	20	+13.47
" C	20	-4.48
" A	30	+23.06
Geppert I.	30	+3.5
" II.	30	+2.6
" III.	30	-5.1
" I.	50	-9.9
" I.	50	+1.8
" II.	50	-3.5
" III.	50	+13.3
" I.	70	-3.7
" I.	70	+3.6
" II.	75	0.
Berg A	92.8	+20.71
" B	92.8	+34.69
" C	92.8	+29.80

V. Effect of Wines.

Person.		Amount of alcohol in cubic centimeters in wine given.	Kind of wine.	Percentage gain or loss in respiration volume.
Weissenfeld	H	7.45	Malt wine	+16.19
"	A	8.5	Sherry	+54.39
"	B	8.5	"	+55.80
"	D	8.5	"	+4.67
"	G	10.25	"	+30.90
"	J	11.0	Malt wine	+14.51
"	K	11.0	"	+22.58
Willmanns	I.	12.0	Sherry	+16.99
Weissenfeld	C	12.75	"	+61.56
"	E	12.75	"	+24.51
"	F	12.75	"	+70.97
Willmanns	II.	22.5	"	+30.60
Geppert	I.	25	Port wine	+9.0
"	I.	60	Cognac	+6.0
"	I.	60	(Rhine wine) (Moussaux)	+15.7
"	I.	75	Cognac	+9.2
Vierordt	A	80	Mosel wine	+0.19
"	B	80	"	-10.71
Geppert	IV.	125	Cognac	-1.3
"	IV.	125	"	+26.7
"	IV.	190	"	+16.2

In his comments on these tables Wendelstadt notes that in the sixty-four experiments a more or less decided increase in the amount of air passing through the lungs was observed in fifty-four of them, a decrease in nine, and no change in one instance; that in the twenty-nine experiments which were made with ethyl alcohol a decrease occurs seven times, while in the thirty-five experiments with wines a decrease occurs only twice; that the average increase after wines is greater than after pure alcohol in equivalent doses, and that the effect of alcohol in non-fatigued persons is often very slight. He also observes that a small part of the observed effect is to be attributed to the sugar and lemon juice used with the alcohol, as was illustrated by a control experiment in which the administration of 100 c. c. of water with twelve grams of sugar and lemon juice resulted in a gain of +1.25 in the respiration volume; but this effect is more than offset by a gradual lowering in the respiration volume, which under normal conditions takes place with the advance of the forenoon. If a correction were made for this normal falling

off, the true effect of the alcohol would probably be found to be larger than is indicated in the tables; that is, the correction would more than offset the error that is introduced by the administration of sugar and lemon juice.

The greater effects of wine as compared with alcohol, in the case of fatigued persons, is clearly seen in the case of Wendelstadt's individuals IV. to VIII. As to the depth of the individual respirations, it is reported that in the case of fourteen experiments on non-fatigued persons an increase in the depth was observed in eleven, and a decrease in three; while in the condition of fatigue the respirations were deeper in ten experiments and shallower in four. The pulse rate was so inconstant in its behavior that no deductions are drawn with regard to this function.

In consideration of the behavior of the more stimulating wines, such as sherry, when given to fatigued persons, Wendelstadt feels justified in concluding that their effect is equally greater in fevers and other states of exhaustion, as frequently observed in the sick, and that the deepening of the individual respirations that results must surely be of benefit to the sick. Our author believes that the action of the alcoholics centres in the central and not in the peripheral nervous system, and that brain workers respond more readily to its stimulating action on the respiration than do those who are employed in manual labor, for the reason that in them the nervous system is in a condition of relative exhaustion as compared with the rest of the body.

It appears to be established then, by a large number of older as well as more recent experiments on men and animals, that alcohol is a respiratory stimulant, even for non-fatigued persons, in the large majority of cases, although it is evident that in many instances its stimulating action is very slight. The latest investigator in this field also admits the truth of this assertion. He, however, attacks the problem from a new point of view and offers a novel theory in explanation of the observed phenomena, his chief object being to learn how alcohol affects the intake of oxygen. Like Binz, Willmanns, Jaquet, and others he makes use of rabbits in his experimental work. His experiments are varied as to conditions. Alcoholic solutions varying from twenty to twenty-five per cent. are employed and are administered by means of the stomach tube only, the volume of the

solution rarely exceeding 30 c. c. A closely fitting mouthpiece serves to connect the animal with the gasometric apparatus. No surgical operations of any kind are performed on the animal.

Careful control experiments were made with solutions of sodium chloride to determine the influence on the oxygen intake of the introduction of neutral fluids into the stomach. The introduction of 25 or 30 c. c. of a physiological salt solution (0.75 per cent.) caused an increase in the oxygen absorption varying from 3.4 per cent. to 6.2 per cent. The introduction of the stomach tube without any fluid, and its withdrawal in thirty seconds, also caused an increase of 4.9 per cent. in the oxygen absorption. In both cases the increase is attributed to an increase in the peristaltic movements of the stomach and intestines, although it is suggested that psychological effects may also be involved.

We have seen that Jaquet bases his explanation of the action of alcohol on the respiration on the fact that all alcoholics irritate or stimulate the walls of the gastric tract, while Binz and his school deny that there is any explanation beyond that of the direct stimulating action on the respiratory centre. Singer's experiments show that Jaquet has exaggerated the influence of gastric irritation and that Binz and his school are right in asserting that a reflex irritation having its seat in the gastric tract cannot account for the increased activity of the respiratory centre. From data obtained by the methods of physical chemistry it was shown that a 13.46 per cent. solution of sodium chloride has the same osmotic tension as a twenty per cent. solution of alcohol. A saline solution of this strength is decidedly irritating to the taste, and the assumption is warranted that it has for the gastric mucosa an irritating action not inferior to that of a twenty per cent. alcoholic solution. Now the experiments on rabbits proved that such saline solutions caused only a slight increase in the oxygen intake as compared with physiological saline solutions, this increase varying from 4.9 to 7.3 per cent.

Taking everything into consideration, Singer concludes that we must make a correction of from 4.7 to 7.3 per cent., or an average of six per cent., in the increase in the oxygen intake caused by alcohol. This correction, expressed in the proper terms, gives the numerical value of the local irritation of the

alcohol in the gastric tract and of the changes induced by the introduction of the stomach tube. Singer then proceeds to show that even small quantities of a dilute alcoholic solution cause a pronounced increase in the absorption of oxygen. Three of his protocols will suffice to illustrate this.

Experiment XIII.

Rabbit, 2320 gms., no food for 20 hours. Injection of 25 c. c. of 3.3 per cent. alcohol = 0.82 gram. Solution at blood temperature.

Normal	O ₂ consumption in 105 minutes	= 2230 c. c.;	in one minute				
		= 21.2 c. c.					
After alcohol	O ₂ " " 60 "	= 1590 " " " "					
		= 26.5 c. c.					
After alcohol	O ₂ in the following 45 "	= 990 " " " "					
		= 22.0 c. c.					

The increase in O₂ consumption, therefore, = 25 per cent. for the first hour after alcohol and for the following three quarters of an hour only 3.7 per cent.

Experiment XIV.

Rabbit, 2635 grams, no food for 12 hours. Injection of 40 c. c. of 2.5 per cent. alcohol = 1.0 gram. Solution at blood temperature.

Normal	O ₂ consumption in 60 minutes	= 1720 c. c.;	in one minute				
		= 28.6 c. c.					
After alcohol	O ₂ " " 60 "	= 2315 " " " "					
		= 38.6 c. c.					
After alcohol	O ₂ in the following 35 "	= 1145 " " " "					
		= 32.7 c. c.					

The increase in O₂ consumption in the first hour after alcohol, therefore, = 34.9 per cent. ; in the succeeding period it = 14.3 per cent.

Experiment XV.

Rabbit, 2320 grams, not starved. Injection of 5 c. c. of 20 per cent. alcohol = 1.0 gram. Solution at blood temperature.

Normal	O ₂ consumption in 60 minutes	= 1535 c. c.;	in one minute				
		= 25.6 c. c.					
After alcohol	O ₂ " " 60 "	= 1875 " " " "					
		= 31.2 c. c.					
After alcohol	O ₂ in the following 60 "	= 1530 " " " "					
		= 25.5 c. c.					

The increase in O₂ consumption in the first hour after alcohol = 21.9 per cent.; in the second hour after alcohol = 0.4 per cent.

An increase in the dose of alcohol did not cause a greater oxygen absorption ; the best results, indeed, were obtained by small doses of weak solutions, as illustrated in the above experiments. After making the necessary corrections, as previously

explained, it is found that a dose of alcohol caused an increase of 20.3 per cent. in the amount of oxygen absorbed in the first hour and of 2.5 per cent. in the second hour after its administration.

Even where a quantity was taken large enough to induce sleep and practically to abolish reflex activity, the observed increase in the oxygen intake still exceeded nine per cent. This fact shows conclusively that the increase in the oxidative activity of the tissues is not to be explained on the assumption of an increase in muscular movements or muscular tension. Narcotics, like chloral, whose full depressant action is always preceded by a period of increased excitability of the central nervous system, appear to act in the same manner. 0.4 gram of chloral caused an increase of 20.3 per cent. in oxygen absorption during the fifty-five minutes following its administration.

In explanation of the observed phenomena Singer offers the opinion that the increased activity of the respiratory centre is not the consequence of a primary specific action of alcohol, but only the natural result of an increased demand for oxygen in the tissues. Alcohol is, therefore, only an indirect excitant of the respiratory centre. It induces the tissues of the body to call for more oxygen, and the respiratory apparatus responds to this call and causes a larger amount of air to pass through the lungs in the period immediately after its administration.

Further experiments, which agree with those of earlier writers, show why alcohol induces the tissues to call for more oxygen. It is well known that alcohol dilates the superficial blood vessels and thus leads to an increase in heat dissipation. Singer's experiments show that this increase varies from 28 to 35.5 per cent. The animal organism counteracts this loss of heat by an increase in heat production. In other words, alcohol induces loss of heat from the body and at the same time causes a compensatory increase in the oxygen intake in order that this loss may be made good by an increased combustion. The sole purpose of the observed increase in the depth or number of the respiratory movements is to furnish the blood with the needed surplus of oxygen.

The fact that weak solutions and small quantities of alcohol led to a greater increase in the oxygen intake than large quantities is explained on the assumption that the former have an

excitant action only, and hence increase the movements of the digestive apparatus and of the skeletal muscles. Any increase in muscular movements must, of course, cause an increase in oxygen consumption.

Some of the most trustworthy work of earlier investigators on the effect of alcohol on the absorption of oxygen stands in agreement with that of Singer. Thus, Wolfers (1883) likewise obtained a decided increase in oxygen absorption in the case of rabbits; also Vogelius, but only after small doses. Geppert's experiments led him to conclude that oxygen absorption is not materially affected by alcohol in the case of human beings, but that it is possible for intoxicating doses to cause an increase, which soon, however, subsides. Zuntz, Berdez, and Henriques claim a moderate increase after small doses in the case of man.

The action of alcohol on the circulation, causing, as it does, dilatation of the superficial, later of other blood vessels, and thus increasing the velocity of the blood flow, or in other words the area of the oxygen-carrying surface, is also in line with the above effects. This action effects the delivery of the surplus oxygen to the tissues.

When all the points bearing on this question are kept in mind it will probably be admitted by the majority of readers that Singer's explanation of the action of alcohol on the respiration is the best hitherto offered. This explanation is certainly of interest and value for the physician, who may well ask what benefit is derived from the administration of an agent which stimulates the respiratory apparatus to handle an increased volume of air merely that the tissues may meet an increased demand for oxygen, a demand which they are forced to make in order to counteract the effects of the increased loss of heat. It is evident that the value of the fraction:

$$\frac{\text{income of oxygen}}{\text{increased need of oxygen}}$$

will determine whether good or harm results from the administration of alcohol. It is difficult to determine the numerical values of these terms, but it will be admitted that in certain cases of lobar pneumonia, for example, those in which considerable pulmonary tissue is engorged and in which the heart is weakened by the toxins present in the blood, income will cer-

tainly not keep pace with the new need of oxygen. An observed temporary improvement in the respiration after alcohol is not in itself sure proof of ultimate benefit.

SUMMARY.

1. Alcohol is a respiratory stimulant of moderate power for human beings. During a period of an hour or more after its administration it causes an increase in the volume of air passing through the lungs and in the absorption of oxygen (3.5 per cent.).

2. Highly flavored wines, brandy, and other alcoholic beverages which contain larger amounts of stimulating esters have a more pronounced action than ethyl alcohol.

3. The stimulating action of alcohol and of alcoholic beverages is greater in the case of fatigued persons than in those who are in no wise exhausted.

4. Increased heat dissipation always accompanies the above-named effects. The compensatory increase in heat production requires an increase in the oxidative processes of the tissues. The increased demand for oxygen is the direct cause of the increased activity of the respiratory centre. Small or "purely exciting" doses of alcohol have also the effect of increasing the movements of the digestive tract and of causing a state of "unrest" or tension in the skeletal muscles, and thus further adding to the demand for oxygen. According to this view alcohol is an indirect stimulant of the respiratory centre.

5. It should be borne in mind that these physiological effects are less pronounced in man than in the rabbit and other animals, which differ from him in respect to the ease with which the respiratory and heat-regulating mechanisms are influenced. Singer's explanation of the action of alcohol on the respiration and on the heat regulating mechanisms of the body at once suggest comparison with one or another of the antipyretics, such as quinine or antipyrin, and call to mind the difficulties that hamper the study of these drugs.

How far the action of alcohol on the central nervous system and how far its influence as a "protoplasmic poison" may modify its operation as an antipyretic; how far variations in the external temperature, in the humidity of the air, and in the temperature of the body itself influence its action must all

receive further study. In a word, detailed chemical and physiological studies similar to those that have been made on other antipyretics are demanded. Such studies will either strengthen or disprove the above theory and will tend to harmonize the conflicting views at present entertained in regard to the uses of alcohol in fever. As the theory now stands, especially when taken in connection with the facts brought out in other sections of this paper, it affords a scientific explanation of the more deleterious effects of alcohol in polar and tropical as compared with temperate regions.

IV. ON THE ACTION OF ALCOHOL ON THE NERVOUS SYSTEM AS STUDIED BY PSYCHO-PHYSICAL METHODS.

The power of alcohol to influence psychical states is among all its properties the most familiar. The effects of the "purple blood o' the grape" are to be noticed at all gatherings of men where wine flows freely. The best-bred man indulging in wine with permissible moderation no more escapes the minor psychical changes induced by it than does its meaner slave fail of its sense-destroying power when he drinks till he "remembers his misery no more." In the case of the former the mental changes induced will never attain the degree when self-respect and social conduct are outraged, and they will pass unnoticed by all except those who are keen observers of their own mental states.

The psychologist James has well said, "The reason for craving alcohol is that it is an anæsthetic even in moderate quantities. It obliterates a part of the field of consciousness and abolishes collateral trains of thought."

The brain is that one among the organs of the body which responds in the most striking manner to the action of alcohol. One need not be skilled in psychology to note the effects of moderate quantities of wine at social gatherings. The speech and bearing of men, the play of features, all bear witness to its power. Restraints are removed, too acute sensibilities are blunted, little acerbities are smoothed down, ideas and mental images follow each other with greater rapidity, a "cerebral sense of richness," and lastly a condition of *euphoria*, a more serene state of consciousness, ensues. All this may perhaps be without detriment to the full intellectual enjoyment of an

occasion, when moderation is the rule. There are many who claim that good wine may properly be used by certain types of mind to deaden nervous irritation, to soothe the over excited, worried, and weary when the day's toil is done.

The world's literature contains ample proof that mankind has sought wine for its influence on the mind. Horace sings:—

“What cannot wine perform? It brings to light
The secret soul; it bids the coward fight;
Gives being to our hopes, and from our hearts
Drives the dull sorrow, and inspires new arts.
Is there a myth whom bumpers have not taught
A flow of words, a loftiness of thought?
Even in th' oppressive grasp of poverty
It can enlarge, and bid the soul be free.”

Brutus exclaims: “Give me a bout of wine. In this I bury all unkindness;” and Richard the Third: “Give me a bowl of wine; I have not that alacrity of spirit, nor cheer of mind, that I was wont to have.”

The psalmist David, in recounting the benefits of Providence, names also “wine that makes glad the heart of man.” On the other hand, all literature witnesses to the terrible evils of the abuse of alcohol. The wise man warns those in authority “Lest they drink and forget the law, and pervert the judgment of any of the afflicted;” and again he says: “At the last it biteth like a serpent, and stingeth like an adder.”

Partridge has pointed out that the pleasure of intoxication, among both primitive and civilized peoples, is due in large part to the wide range of the emotional tone; the psychological changes of the state show an increased activity in those sensations, emotions, and associations which make up the self, and the increased social feeling is secondary to and dependent upon these changes. He also points out that intoxication with one agent or another is one of the important parts of the religious and social life of primitive man; that the drugs used for this purpose are capable of increasing or decreasing the *intensity* of consciousness; that the historical importance of intoxication is shown by the deep impression it has made upon literature and language; that a study of analogues of the intoxication state shows that there has grown up in the race a strong impulse to see intense states of consciousness, and that this impulse has been favored by natural selection for various reasons.

Primitive man is not a steady nor habitual drinker, but his periodic intoxication is characterized by great excess and violent, uncontrolled excitement. An increasing regard for the self, an increasing interest in general self-control as an ideal, is certainly, as Partridge points out, a most potent factor in the development of temperance.

If it is admitted that psychical processes are influenced by moderate and non-intoxicating quantities of alcoholic beverages, we may pass on to a closer analysis of the cerebral action of alcohol and may consider such questions as whether it is to be regarded as a "cerebral stimulant" or the contrary, and whether it can be used in small quantities without detriment to the mental processes, when taken in their entirety.

According to Lussana and Albertoni, alcohol affects the brain in a noticeable manner when the dose reaches 0.4 parts per thousand parts of body weight; that is, nine ounces of wine containing ten per cent. of alcohol suffice, when taken by an individual of average weight, to induce cerebral changes that can be made the object of study. A much smaller quantity suffices in one unaccustomed to the use of alcohol in any form to bring about changes which are appreciable to his own consciousness. Popular usage applies the term cerebral "stimulants" to the usual alcoholic beverages, but it is more than doubtful whether this term can properly be applied in view of the results of the existing psychological experiments which have been made with alcohol and its pharmacological congeners, paraldehyde, trional, chloroform, etc.

When we consider what are the purely physiological and psychological phenomena of the early stages of alcoholic intoxication, it is not surprising that the uncritical observer should use the term "stimulant" with reference to alcohol. It is especially in those individuals who are unaccustomed to its use, and who possess an excitable vascular apparatus, that the appearances of so-called stimulation are manifest. In such the face and upper parts of the body are more suffused with a pink color, the eyes are more brilliant, a sensation of warmth is experienced on the surface of the body and in the stomach, the sweat, salivary, and gastric glands are somewhat stimulated, the pulse is fuller and faster, gestures and muscular movements in general are more frequent and pronounced, and the respiration

responds by an increase in rate and depth. Both wine and environment supplement each other in producing the emotional and intellectual effects already alluded to, and which at first sight may well appear to be the results of a true stimulation of the cerebral faculties, the circulation, etc. A number of investigators in the field of pharmacology, notably Mitscherlich, Schmiedeberg, Filehne, and Bunge, declare emphatically that alcohol is not a cerebral stimulant, or at best deny that there is any proof that alcohol is a cerebral stimulant. Schmiedeberg declares that its stimulating action is only apparent and not real, that its primary action is a depressant one for certain higher and more easily influenced brain processes, that some functions of the brain are weakened or paralyzed before others, and that one of the first consequences of this condition is the loss of the finer shades of restraint. The so-called "excitement" is only the expression of a more or less marked incoordinated activity of the psychical activities. The restraints of reason and judgment are removed by the anæsthetic power inherent in alcohol, and thus troublesome and minute indecisions fall away, motor activities in the form of speech and gesture are freer and less hampered, and the behavior of the individual leads the superficial observer to assume that his brain is being "stimulated." The self-deception which is so apparent to the onlooker, in regard to the individual's own physical and intellectual ability, his false estimates of his body temperature and reaction time, and many other physiological processes, are all adduced by this school as further proofs that alcohol is a paralyzant rather than a stimulant for the brain. It is further sought to strengthen this opinion by pointing out that alcohol is a depressant of such physiological activities as are involved in maintaining the body temperature, the circulation, and the respiration. In a word, Schmiedeberg and his school refer every alteration in the field of consciousness to a primary paralytic action of alcohol, however elusive to analysis and detection this paralysis may be. The "stimulation" of the emotions and faculties is but "fictitious and is in reality due to the removal of the barriers of self-restraint by the paralysis of higher functions."

It is evident that we have entered the field of the experimental psychologist. He alone can tell us whether this opinion

of the pharmacologists is tenable. As this field of research lies outside of the writer's personal knowledge, he must enter with some diffidence on a summary of the work of psychologists and physiologists in regard to alcohol.

Some of the earlier experimenters in this field endeavored to learn whether alcohol lengthens or shortens the time that elapses between the moment when the mind perceives a given stimulus, such as a mild electric shock, and the execution of a responsive movement, which by prearrangement should immediately follow the sensation. Such an experiment is called a simple reaction experiment or an experiment on the reaction time from hand to hand, eye to hand, ear to hand, etc., as the case may be. The experiment is by no means as simple as it would appear; the perusal of a modern work on experimental psychology will convince the reader that the reaction consciousness is made up of a number of stages and that the reaction must be studied both on its "sensorial" and "muscular side." Psychologists furthermore inform us that "absolutely irreproachable experiments on reaction time are not easy to carry out," and it will not surprise us to learn that no entirely concordant results as to the influence of small quantities of alcohol on the simple reaction time have thus far been obtained.

In Exner's experimental investigation of simple psychical processes made in 1873, an experiment is described which proves that a large quantity of wine lengthens the reaction time from eye to hand very decidedly. An electric spark served as a stimulus for the eye, and the reactor was obliged to press down on the lever of a registering instrument with his right hand the moment the light of the spark was perceived. Only large quantities of wine were taken, and it was found that the average reaction time of 0.1904 second, from eye to hand, was lengthened to 0.1997 second by one bottle of Hochheimer, and to 0.2969 second by two bottles. A glass of beer, however, quickened the reaction time from the left hand to the right hand, an electric shock being the stimulus applied, from 0.1751 to 0.1706 second.

A few years later, 1877, Dietl and Vintschgau made more extensive experiments on the influence of morphine, coffee, and wine on the reaction time from hand to hand. In these experiments the stimulus was the application of a light brush or of a

mild electric shock to one of the fingers of the right hand, and the responsive signal was made by depressing an electromagnetic marker with the same hand. Quantities of champagne and of Tyrolese table wine, varying from one third to one bottle, were taken, and the reactors concluded that small quantities of wine caused a shortening of the reaction time, which persisted for a considerable time if the wine was taken gradually in small quantities; but that when larger quantities were taken in a short space of time a decided lengthening of the reaction time was the result.

Later investigators, such as Kraepelin and Warren, have criticised this earlier work, claiming that the experiments are too few in number and that the variations among the averages, independent of an alcohol effect, are too great to make any inferences possible.

Warren (1887) has made more than 8000 observations on the influence of alcohol on the time which elapses between the stimulation of one or two fingers of the left hand, by an induction shock of moderate intensity, and the closing of a simple key, like the ordinary telegraph key, by the right hand. Moderate quantities of pure ethyl alcohol in ten per cent. solutions, equivalent to from one seventh to one half a bottle of champagne, were administered to the persons experimented on. Warren was unable to draw any definite conclusions from his long series of reaction times. He says, "The changes in the reaction time after taking varying amounts of pure alcohol are, on the whole, more considerable than those occurring in equally long experiments without alcohol. There is no obvious and unquestionable relation of the effect, in quality or in quantity, either to the amount of alcohol taken or to the time during which its influence has been exerted."

Kraepelin, whose experiments (1882-92) on the influence of alcohol on both simple and more complicated reaction times preceded those of Warren, claims to show that moderate doses of alcohol (15-30-45 grams) shorten certain reaction times quite appreciably during twenty minutes following the administration. Kraepelin claims that Warren frequently neglected to test his subjects in the interval *immediately* following the administration of the alcohol and also tries to show, on other grounds, that Warren's experiments really support the view

advocated by himself. According to Kraepelin, both the time required for a simple reaction and that required for what is known as the "choice reaction" is shortened by alcohol. In arranging the experiment for the study of this reaction "the reactor is told, for example, that he will be shown either black or white and that he is to react only when he has cognized the black as black or the white as white. But further, he is to react to black by a movement of the right hand and to white by a movement of the left hand." (Titchener.) In this form the choice reaction is an example of selective action; a conflict of impulses is introduced into the experiment.

Kraepelin agrees with all previous observers in ascribing to larger quantities of alcohol a slowing action on all forms of the reaction time.

A psychologist, reporting in the "American Journal of Psychology" on Warren's experiments, says that "these experiments were made before attention had been called to the distinction between what Wundt calls *motor* and *sensory* reactions; that is, between those that are automatic and those that are accompanied by full psychic processes. The figures found for the normal reactions, from 0.1398 to 0.2001 second, would mark them as of the intermediate or mixed class, from which uncertain results are apt to follow. The action of the stimulant in inclining the subject toward the motor or sensory form is not known; it may differ from subject to subject or even with the same subject at different times."

On examining Kraepelin's tables it becomes evident that there is an appreciable shortening of the simple reaction time in all those experiments in which the *normal* values for the reaction times of certain individuals coincide with the figures usually given for the motor form ("muscular reaction" to pressure, sound, etc.). In these parts of Kraepelin's tables the normal reaction time varies from 0.129 to 0.153 second; after alcohol (twenty-five to forty-five grams) it varies from 0.112 to 0.148 second.

When we take into account, as shown by other psychological experiments, especially in reference to certain forms of the association reaction, that alcohol favors the liberation of motor impulses, we may well believe that the average duration of the muscular reaction to stimuli is shortened for a brief period suc-

ceeding the administration of a small quantity of alcohol. This shortening of the reaction time would be more marked in individuals of the "motor type." The reader may be reminded at this point that Wundt's separation of the ordinary simple reaction into a motor and sensory form is not accepted by all psychologists. For the opposition to this view the writings of Baldwin may be consulted.

Kraepelin's discussion of his own results shows clearly that in all those forms of reaction in which the reactor is obliged to dwell on or to compare the sensations a lengthening of the reaction time occurs.

The influence of alcohol on other mental processes has also been studied by Kraepelin. He finds that the time that is required to find a word that will rhyme with a given word is shortened, and that the period of time during which this shortening of the reaction time occurs continues for a considerable period after the alcohol has been taken.

In this form of the "partially constrained" association reaction it was noticed that the reactor's mind made great use of concepts based on the tone and movement consciousness. It is to be noted that the "association" was not constrained or held to a logical connection between word and fitting rhyme; and while the results are very interesting, it is hardly probable that rhymes written with greater speed under the influence of alcohol are poetically superior to those constructed without the help of this stimulus.

On the other hand, Kraepelin found that the time required in that type of the constrained association reaction which includes the formation of a subsumption judgment is hardly at all shortened.

Another process which is slightly hastened by alcohol is reading in a whisper,—more words can be articulated in a given time; here, too, there is a readier liberation of motor impulses. The time required to learn by heart columns of simple figures is somewhat shortened by alcohol. The time required to add columns of figures is, however, lengthened by alcohol and shortened by tea.

Kraepelin concludes from the numerous psychological experiments made by him that those psychical processes which involve the liberation of motor impulses are for a short time hastened

by small quantities of alcohol, such as would be represented by one fourth or one third of a bottle of claret or hock. Examples of these processes are the simple motor, the choice reaction and association reactions involving sounds. On the other hand, those processes which involve the reception and mental working up of conceptual material, like the addition of figures, are affected in a detrimental manner from the very first by alcohol. In other words, alcohol, according to Kraepelin, exerts a "stimulating" action on the organ of mind when it is occupied with sensory-intellectual material, but has a depressant action when the mind is engaged in purely receptive or constructive operations. Larger quantities of alcohol, say the equivalent of a bottle of ordinary wine, depress every type of psychical energy from the very first.

It is not without interest in this connection to cite the testimony of that master mind, Helmholtz, who declared that the smallest quantity of alcohol sufficed to dispel from his mind every idea of the creative order when he was trying to give form and being to some dimly seen conception.

It merely remains to mention that the protocols of the researches that have been cited frequently give instances of the false subjective estimates made by the reactors under the influence of relatively large quantities of alcohol. The reactor often believes that he is reacting more quickly than under normal conditions, while in reality this reaction time is longer. The opposite state of affairs is also occasionally met with.

Some time after this article was completed the valuable and interesting paper of S. E. Partridge, entitled "Studies in the Psychology of Alcohol," made its appearance. Among other things Partridge has studied the effect of small quantities of alcohol upon the rapidity of adding, reading, and writing. The experiments on these processes were made by Partridge upon himself and covered a period of thirty-three days. The amount of alcohol taken was ninety grams of $33\frac{1}{3}$ per cent., and it was consumed at 7.55 A. M. Work was begun at 8 A. M. and was continued until 10 A. M. The tests occupied approximately seven minutes of a ten-minute period, the remainder of the period being given to rest. "For adding, sheets containing sixteen columns of figures, twenty-five in each column (400 in all), were used, the same sheets being used each day, but in a

different order. The reading test consisted of reading audibly, at a maximum rate, the figures which had just been added. For a writing test digits from one to nine were written at a maximum speed, preliminary practice having been made in order to acquire a uniform movement."

"The average adding time for the whole series is, normal, 162.3 seconds (mean variation 7.4 seconds), after alcohol it is 160.9 seconds (mean variation 6.9 seconds), for the first hour the normal is 163.0 seconds (mean variation 7.0 seconds); after alcohol 161.2 seconds (mean variation 8.7 seconds); for the second hour the normal is 161.7 seconds (mean variation 5.6 seconds)." The effect is evidently slight and is rather in the direction of quickening the process than the reverse, and lasts nearly to the end of the second hour. In the case of the reading the effect of the alcohol is first a quickening and then a slowing, both changes being insignificant and mutually compensatory in the general average. The reading time was subtracted from the adding time in order to obtain approximately the time consumed by the association process in adding. The averages for the whole series showed that the association process involved in adding was quickened.

In the writing test the effect of the alcohol is also hardly perceptible, but in so far as it appears it consists in a quickening of the work during the first hour, followed by a slowing during the second hour. As regards the *quality* of the work the results are declared to be uncertain.

In his summary Partridge points out that the effects of about three ounces of $33\frac{1}{3}$ per cent. alcohol, taken under the conditions described, made only a slight difference in the psycho-physical tests; that in the adding, which is mainly an association process, the slight quickening lasted nearly to the end of the second hour; and that in reading and writing, which involve more muscular action, the effect is comparable to that observed in experiments with the ergograph in that the preliminary quickening is followed by a period of retardation.

The different psychological standpoint of Partridge as compared with Kraepelin is brought out fully in the following passage from the former author's summary of his results:—

"These results do not confirm Kraepelin's conclusion that the 'sensory' process (adding is regarded by him as a 'sensory'

process) is depressed by alcohol from the start, while the motor process alone is at first stimulated. In fact, the opposite seems to be true. The association process is quickened, while the motor processes appear to be more likely to be slowed by the alcohol. It could not be discovered in any case that the repressing effect of the alcohol persisted until the following day." Partridge remarks in another section of his paper that the tables of Kraepelin sometimes show a shortening of the association time as an initial effect.

We have thus far dealt only with the effects of alcohol administered in single doses, but we have also to consider the action of repeated doses.

Smith has studied the action of alcohol, when administered for a number of weeks in small doses in quantities varying from forty to eighty grams *per diem*, in its influence on the simpler psychical processes. This investigator found that there was a decrease in the ability to add figures, amounting in twelve days to about twenty per cent., while the power to memorize was diminished by about seventy per cent. The action of alcohol as affecting reaction times and "associations" was also studied. During the first few days of the alcohol periods there was the usual occasional occurrence of premature responses; later the reaction times were lengthened. Among the associations there was a decrease in the number of those classified by Wundt as "inner" associations and an increase in the number of "outer" and sensorily disconnected associations. "Inner" associations are interpreted as a higher form of intellectual operation than the two other classes named. The damaging action of the alcohol was sometimes apparent on the very first day; sometimes only on the second day of the alcohol period. No experiments were made until from eight to twelve hours after the last administration of the alcohol, and the influence of the acute or immediate action of alcohol as illustrated in Kraepelin's experiments does not enter into Smith's results. The conclusions are drawn that one half to one bottle of wine, or two to four glasses of beer, a day not only counteract the beneficial effect of "practice" in any given occupation, but also depress every form of intellectual activity; that every man who, according to his own notions, is only a moderate drinker places himself by this indulgence on a lower intellectual level

and opposes the full and complete utilization of his intellectual powers.

It is to be regretted that the influence of one fourth of a bottle of wine or of one glass of beer a day — that is, quantities which are consumed by many very moderate drinkers with apparent benefit to mental and physical health — were not studied by Smith. It does not follow that if one bottle, or even one half bottle, of wine a day has an appreciable effect on intellectual performances one fourth of a bottle will also have an effect.

Partridge has also given a summary of experiments made by him on a number of individuals with *intoxicating* doses of alcohol, which may be presented at this point.

“Experiments which were made by the present writer upon four subjects with intoxicating doses of alcohol show that until the intoxication is well advanced the rapidity of simple mental processes was not greatly decreased. Adding, the memory of nine place figures, rapidity of tapping, strength of hand clasp, estimation of distance and of time, and clearness of vision were not seriously interfered with until muscular incoördination became extreme. The rapidity of tapping was most affected. Ability to control a reflex wink was greatly increased by the alcohol. A study was made also of the effect of intoxicating doses of alcohol upon the association of ideas. A list of 400 words was given to the subjects, once on a normal day and then again two weeks later, during the stages of a progressive intoxication. A single reaction to each word was required and the time was not taken. Comparing the two series of normal and alcoholic reactions, it appears that in the case of each subject there was a progressive dissimilarity in the two series which reached a maximum and then decreased as the effects of the alcohol passed off. The most noticeable change in association was the increase in the egoistic associations due to the alcohol. In one case the visual associations were increased. The chief effect upon consciousness was a succession of changes in the emotional tone. In all cases a stage of exhilaration was followed by a stage of depression and melancholy, which in turn gave way to the normal condition. In two cases a second stage of exaltation followed the melancholy stage, but this was not so clearly marked as the first period. The emotional changes

seemed to dominate the changes in the character of the associations. In each case there was a very clearly marked moment in which there was a feeling that control was being lost, accompanied by a desire to throw off all restraint and give way to the feelings."

It is universally admitted by medical men that alcohol in any form is deleterious to the growing organism. Demme recounts an interesting experiment which was made by two gentlemen of Berne, Switzerland, who were believers in the beneficial action of moderate quantities of alcohol. Wishing to see for themselves whether alcohol really affects the power of attention, the memory, etc., of children, they made the following experiments on their own sons, whose ages ranged from ten to fifteen years. The younger lads received about 70 grams ($2\frac{1}{3}$ ounces) of wine, which was taken diluted with water at both the noon and evening meals; the older boys received about 100 grams ($3\frac{1}{3}$ ounces) at each meal. The experiments were carried on for a year and a half in such a way that a period of several months of use alternated with several months of abstinence. The results of the experiments were, that during the wine periods the children were more languid, more sleepy, and less inclined to perform mental tasks. Their nights were more restless and their sleep less refreshing. Two of the lads were so much impressed by their lack of "condition" during the wine period as compared with the no-wine period that they begged to be excused from further wine drinking.

It is not the purpose of the reviewer to treat either acute or chronic alcoholic intoxication from a psychological point of view. Numerous writers on mental pathology have drawn analogies between these conditions and various forms of mental diseases.

It may be pointed out, however, that the psychological experiment in its various forms has been made use of by Fürer to analyze the after effects of a "spree," and that Nadler has studied in the Yale Psychological Laboratory the reaction time of fifteen individuals on the verge of delirium tremens, both before and after they had been put through a course of treatment. Fürer's experiments were made with himself as the subject. When he became drunk in the morning the psychical after effects, as shown by experiments, were noticeable during

the whole of the following day; when he became drunk at night the after effects were still plainly noticeable, in the experiments made, on the evening of the day following. Among the results of the various experiments made by Fürer attention may be called to the fact that there was a diminution in the power to add figures, though this was less pronounced than the depression of other forms of mental activity. The power to memorize columns of figures was decidedly weakened. As Fürer learns by heart in accordance with the "psychomotor" type, it is apparent that the after effect of the intoxication was to render more difficult the fixation of psychomotor memory contents.

Nadler's experiments with men on the verge of delirium tremens were made at a time when the mind of the subjects was clear and active. They were utterly worn out, acutely anxious, suffered from loss of sleep, and had tremors and a shaky walk. The simple reaction times were found to be considerably shorter than in any series of experiments performed on healthy persons; the complex reactions, though, were found to be longer, that is to say, "the differences between the simple reaction times and the complex times are longer than for the normal person. In the experiments made upon the same individuals after treatment the results showed a decrease in the reaction times throughout, making the simple reaction times less than in the normal and the complex times about normal. These results appear to show that the effect of the alcoholic toxine upon the individual is to heighten the power to perform simple regular movements, but that where a judgment is needed the individual is at a disadvantage."

In concluding this section of our review we may ask whether the results of Kraepelin and of others, which for the present must be accepted as showing that certain more elementary mental processes are hastened — that is, that the brain is "stimulated" for a time by alcohol in the performance of operations of a lower order — are incompatible with the belief that alcohol is in reality a depressant and that the greater motor facility is simply the consequence of a primary paresis of governing "centres." Kraepelin himself discusses this point and comes to the conclusion that the greater motor facility is caused by a stimulating action of the alcohol. His arguments are largely

based on examples drawn from the field of mental pathology, and he gives plausible reasons for believing that a state of "motor excitability," of mental exhilaration, fleeting ideas and images, and belief in superior mental power may coexist with an undiminished power of perception and judgment in regard to external conditions.

It would seem to the writer impossible to arrive at a positive conclusion as to the point at issue at the present moment. Those who assume that the psychological results obtained by Kraepelin are best explained by assuming the removal of restraining or inhibitory functions in consequence of a primary paralyzing action of alcohol can furnish plausible arguments by analogy in support of their opinion.

In all its lower physiological activities the central nervous system not only arouses organs under its control to action but also restrains or inhibits them. Remove or paralyze the inhibition and excessive activity is the result. The nervous control of the heart and respiration and the reflex activity of the cord are but a few among many instances. Physiologists have shown that not only the cerebral cortex, but also the subcortical centres, are endowed with a stimulating and an inhibiting power for the muscles of the body. As to the mechanism of the inhibition of voluntary acts, physiologists are not agreed. Some, like Meltzer, assume that the voluntary interruption of a voluntary movement is accomplished by the aid of the antagonistic muscles, though he does not deny that an inhibitory mechanism may be made use of in this act. Sherrington, however, has made experiments on the muscles of the eye which appear to show that the mind, in interrupting voluntary movements, makes use of an inhibitory mechanism governing the tonus of the contracting muscles.

James, in speaking of the inhibition of one cerebral process by another, says: "*We should all be cataleptics, and never stop a contraction once begun, were it not that other processes simultaneously going on inhibit the contraction. Inhibition is, therefore, not an occasional accident; it is an essential and unremitting element of our cerebral life.*"

Meltzer records a number of instances, drawn from the work of Setschenow, Urbantschitsch, and Exner, "which would seem to demonstrate the actual existence of a central as well as a reflex inhibition of sensations."

If we assume that a restraining factor is an inseparable part of the cerebral processes concerned in voluntary motion and in the reception of sensations, we must be prepared to accept the opinion that damage done to the restraining mechanisms by a sedative agent like alcohol may be followed by greater freedom and quickness of motion, by a more intensely or more quickly cognized sensation.

The reaction consciousness in the case of "muscular reaction," for example, is made up of the

- (1) idea of end and idea of movement ;
- (2) idea of end, and idea of movement, and idea of object ;
- (3) sensations set up by movement.

Here, then, are several factors, — voluntary movement, sensations, etc., — in all of which inhibition may as truly have a hand as it does in regulating the movements of the heart. Weaken inhibitory control of one of these factors and you may well have a shortening of the time of the total reaction. We shall learn, when we study the action of alcohol on the circulation, on metabolism, etc., that its action in those fields is rather of a depressant than of an excitant order ; and psychology may yet see its way to an explanation of the increased cerebral motor activity after alcohol, by the assumption of a paralysis of inhibition, rather than a direct excitation of the "centres" immediately concerned.

Experiments on the influence of alcohol on the so-called "muscular sense" and on the special senses have also been made.

Jacobj (1893 and 1894) has made experiments on the influence of alcohol on our ability to estimate differences of weights and has constructed an apparatus which he calls an effort scale, by means of which weights of different denominations may be compared. The weights employed are not touched by the subject of the experiment, but are raised by grasping a vertical handle connected with a lever, which carries them. The forearm is kept approximately at right angles to the body, while the hand grasps the handle ; the same set of joints is always used, and their movements are similar in a normal series of tests and in a series after alcohol. The disturbing influence of pressure sensations is supposed to be reduced to a minimum. Surprisingly enough, Jacobj finds that small differ-

ences in weights are estimated more accurately after a small quantity of alcohol than when no alcohol is taken. According to this investigator, this result is not brought about by a stimulating action of alcohol, but rather by a paralyzing or sedative action on one of the cerebral processes involved in the final judgment.

The writer offers no criticism on Jacobj's reasoning, but would point out that he is at variance in some of his premises with the ideas accepted by most psychologists. Thus, he affirms that sensations arising from the tension of tendons have, as such, no influence on the formation of a judgment of the difference between two weights.

He assumes that this judgment is formed as the result of a mental comparison of the *amount of innervation* expended in overcoming the resistance offered, with the *time* that elapses between the moment of the outgoing muscular impulse and the actual occurrence of the resulting movement. This interval of time is spoken of as the latent period. When the latent period reaches a certain minimum the ability to distinguish differences in weights ceases. Alcohol, by its sedative action on the organs of innervation, is supposed to prolong the latent period; and as this now rises above its normal minimum value, an estimate of a difference in weights, normally inappreciable, is now possible. Larger quantities of alcohol not only prolong this latent period but also depress mental functions in general to such a degree that "discrimination" is paralyzed and the ability to differentiate weights falls below par.

If the reader will compare Jacobj's explanation of the mental factors involved in the exercise of the so-called muscular sense with that offered by Külpe and other modern psychologists, he will note serious discrepancies between the two. Most psychologists and physiologists deny that a sensation of an afferent discharge from the brain to the muscles is a factor in our judgment of differences of weight; many, indeed, deny the existence of such a sensation.

Waller correctly says that "by muscular sense is denoted a sum of sensations, derived from the varying tension and pressure of all the motor organs and of the skin, caused by movements. In any complete analysis of the phenomena the first problem is to separate the cutaneous component; the next is to separate

the residue into its muscular, tendinous, ligamentous, and articular components." In summing up the results of an experimental and critical study of the sense of effort, Waller further says: "In sum, the view which I am inclined to take is that the duly coördinate action of the muscular executive depends upon three factors: (1) Upon coördination at the central origin of action, which coördination is the resultant of past experience and consists in the emission of nerve impulses grouped and measured in conformity with intended and foreseen effects.

"(2) Upon appropriate and corrective reflex response of which the immediate causes or stimuli are centripetal impulses from sense organs, inclusive of those less obvious impulses from the skin, muscles, and articulations which are collectively referred to a muscular sense.

"(3) Upon direct muscular response to passive stretching and extensile vibrations."

Jacobj's experiments deal with muscular sense phenomena "in the lump," to borrow Waller's expression; and while his supposition that the amount of central motor innervation (*Innervationskraft*) plays a rôle in the judgment as between two weights would find a supporter in Waller, it is nevertheless evident that many more factors are to be considered. Further, Jacobj's assumption that alcohol in small amounts, from the very first, paralyzes central innervation, is perhaps not sufficiently fortified by examples; and we must rest content to accept his facts, and leave the future to decide whether his explanation of them is the correct one.

J. J. Ridge (1882) has also published a few experiments on the influence of alcohol on our ability to discriminate between weights; but his actual results are the opposite of those obtained by Jacobj; that is, he finds that the power of discrimination for weights is decidedly diminished by both small and large quantities of alcohol. Ridge's paper contains only a meagre description of the method employed, and it is impossible to judge to what extent the senses of sight, strain, and pressure, were involved. The observations are few in number, and their probable error was not calculated, and subjective factors were not eliminated. Ridge describes his apparatus in the following words: The tests were made "by an arrangement in which a weight was attached to a certain lever, and the person experi-

mented upon was required to slide an equal weight along another lever exactly similar to the first, until in his opinion the weights appeared to be the same. It is obvious that the position of the weights on each lever ought to be exactly the same; and, therefore, the more sensitive the muscular sense, the nearer will the individual be able to place them, before he ceases to detect any difference." Experiments were made on three non-abstainers, and on seven abstainers; and the quantity of alcohol administered varied from one half to four drachms, diluted with at least three times its bulk of water. The general average in the distance between the weights was 5.105 mm. before alcohol, and 7.095 mm. after alcohol. Some of the trials after alcohol gave more accurate results than some of those before it; but the average of each individual was found to conform to the general average of the whole. When the criticisms made above are borne in mind, it will be seen that Ridge's experiments are of no value.

A few experiments have been made on the effect of alcohol on the acuteness of the localizing perceptions of the skin for distances between compass points. F. Kremer (1884) found that the discriminative ability of the skin for points was decidedly lowered in a young man after he had taken sixty grams of alcohol. On the thighs, the sensitivity fell from 4.2 to 5.8 cm. on the anterior part of the leg, just below the knee, it fell from 3.2 to 6 cm. The lowered sensitivity of the skin was perceptible in ten minutes after the administration of the alcohol; and Kremer sees in this quick result a proof of the rapid and considerable action of alcohol on the nervous system.

Lichtenfels had in 1851 arrived at the same conclusion. In experiments on himself and on Fröhlich, he found that the dorsal surface of the forearm could plainly discriminate compass points which were 34 mm. apart; but after alcohol, the points had to be 55 mm. apart before they were perceived as separate points. This result was obtained ten minutes after taking forty grams of absolute alcohol, dissolved in 160 c. c. of water. One hour after the alcohol was taken, the distance between the points had to be increased to 60 mm. It is to be noted that the quantities of alcohol used by these investigators were large enough to cause "a very noticeable degree of narcosis," to cite the words of Lichtenfels. Neither Lichtenfels nor Kremer

takes any account of the influence of the flushing of the skin vessels on the discriminative power of the skin. According to Alsberg, both hyperæmia and anæmia of the skin lower its ability to discriminate points.

Ridge also claims to find that touch is less acute after alcohol. In Ridge's work the disturbing influence of other senses is not excluded; the subject of the experiment himself moved a rack and pinion apparatus in order to approximate one point to a spot equally distant from two outside points, the distances to these two points being estimated by the forefinger. The final word as to the value of these experiments must be left to the modern psychologist.

E. E. Smith is often cited by uncritical writers on the action of alcohol, as having shown that this agent, even in small quantities, lowers the acuteness of touch, sight, and hearing. I cannot find that this author has made any psychological experiments which warrant these statements. Smith's words, as taken from his memoir on the action of alcohol on the respiratory process, as published in the "Philosophical Transactions," vol. 149 (1860), page 732, are as follows: "The early effects of large quantities of various alcoholic beverages consist of lessened consciousness, with cloudiness, swimming, or giddiness, beginning in less than ten minutes, during about thirty minutes; lessened sensibility to light, sound, and touch; wavy or buzzing sensations passing through the whole body; and a semi-cataleptic state, in which there was indisposition to move any part of the body from the existing position," etc.

It is evident that this description of subjective experience during intoxication cannot serve to illustrate the action of small quantities of alcohol on the acuteness of the senses, and they should not be cited as doing so.

Fröhlich (1851) has made experiments on the influence of alcohol on the sense of smell. The quantity of alcohol consumed was large, 200 c. c. of a forty per cent. solution; and its narcotic effect was perceived after ten minutes. When tested ten minutes after taking the alcohol, the subject believed that he was better able to appreciate pure odors, like that of oil of bergamot, musk, etc., than in the period before alcohol; but his sensitivity for such things as ammonia and chlorine, which have an irritating quality in addition to their smell, was decidedly

lowered. After the lapse of fifty minutes the reactor found it difficult to differentiate substances with pure odors which are closely allied, and a longer time was required to form a judgment as to a given odor of pure quality; and at this time vapors of ammonia, which was sufficiently strong to cause frequent sneezing, could hardly be detected.

Although the amounts of alcohol taken by Lichtenfels and Fröhlich were rather large, their experiments fall in line with practical experience. It is stated that tea-tasters, smelling experts in oils, essences, and perfumes, and wine and liquor testers, find that an indulgence in alcoholic beverages, which would not seriously incapacitate them for other duties, seriously interferes with the excellence of their peculiar kind of work. In an explanation of this fact, the local action of the alcohol on the throat and mouth would have to be considered as well as its cerebral action.

As to the influence of alcohol on the sense of sight, but little work has been done. Ridge has made some experiments, by which he claims to have shown that, after the administration of a little alcohol, a number of letters arranged in different ways were not made out as well as before alcohol; and that the distance between the reader and the letters had to be shortened by nine per cent. before the letters could be read. These experiments are of no value. Subjective influences were not eliminated, and the observations are few in number. No attempt is made to estimate the probable error in the several observations, and sufficient importance is not attached to the great variability of the results before alcohol.

Of greater value are the experiments of W. Reis (1895) on the influence of wine and pure alcohol on the power of eye measurement. This investigator's apparatus consisted of a strip of wood exactly one metre in length, whose divisions were marked on the opposite side from the observer. An assistant moved a sliding marker until the subject of the experiment believed that the pointer had reached the middle point of the strip. Equal illumination of the two halves of the bar, and good light for the observer, were among the many precautions taken. Ten readings were taken during each trial, and the pointer was started alternately from the right and left ends of the bar. The mean variable error, f , for each act of ten trials,

was calculated by the method of Gauss; and the value of this error in the normal state was compared with its value after considerable quantities of alcohol or wine. In the first experiment, the normal value of f was 0.19 cm. Fifteen minutes after Reis had taken 80 c. c. of ninety-five per cent. alcohol, properly diluted and sweetened, f was found to have risen to 0.44 cm.; and one half hour later its value was 0.40 cm. Twenty-five minutes later, a second dose of alcohol equal to the first was taken. This second dose at first raised f to 0.46 cm., and later to 0.90 cm. No readings were taken after the symptoms of mild intoxication appeared. The remaining experiments with pure alcohol gave similar results, all proving that the mean error of eye measurement is greatly increased by pure alcohol. The experiments with wine were six in number; and for each experiment a bottle of good, properly aged wine was drunk. In these experiments the mean error was not increased as much as when an equal amount of pure diluted alcohol was taken. Thus, in one experiment, the normal value of f was 0.10 cm. and attained the value of only 0.42 at its highest, after one entire bottle had been consumed in the course of three quarters of an hour. In a second experiment f rose from 0.17 to 0.64 cm.; in a third, from 0.20 to 0.69 cm. Morphine, paraldehyde, amylene hydrate, and chloral, all rivaled or even excelled alcohol in their ability to raise the mean error. Tea actually somewhat lowered the error of reading, thus exerting a favorable action on the judgment. Acetic ether, as representing substances to which wines owe their bouquet, caused only a slight rise in the mean error.

Reis claims for good wines a position between the narcotics, pure alcohol, and the volatile esters, and concludes that they cause only a comparatively slight rise in the mean error of eye measurement. That wines act more favorably than alcohol in equal quantity is perhaps to be referred, to some extent, to the esters contained in them. This investigator is hardly justified in minimizing the sedative action of wines for eye measurements, as he does in his summary; for his protocols, as already quoted, reveal a not inconsiderable increase in the mean error. Reis points out that expert riflemen avoid alcohol during their performances. Greely relates that "At Sabine the issue of alcohol in the morning to hunters on urgent medical recom-

mentations was followed by the Esquiman Jens, an unerring hunter, missing, at his own chosen distance, a large seal which might have saved the party; afterward, Long, his nerves unaffected by spirits, killed, at the water's edge, a bear over two hundred yards distant." Not long ago I attended a sportsman's tournament; and happening to come upon the experts who were pitted against each other in a "live-bird match," was struck with the quick and accurate shooting of a man who, on inquiry, was found to be a shot of national reputation. After this man had not missed a bird during some twenty odd shots, I observed that he laid down his gun, and went to the building containing the bar-room; I followed and observed him in the act of tossing off a glass of whiskey. Once more, an hour later, he made a trip to the restaurant. The effect of the whiskey was soon shown by numerous misses; and at the close of the day's shooting this man was fourth in the list, the first prize having been won by a stolid-looking man, who made no trips after whiskey. Neither this nor Greely's incident is advanced as a case which verifies the laboratory experiments of Reis, as it is possible that other factors of one kind or another had an influence on the result. I can but regard it as very probable, however, in view of practical experience, that the alcohol was to blame in both cases. I have no doubt that the same prohibition also holds for billiard playing, tight-rope dancing, and the arts of the juggler, all of "which demand the most delicate appreciation of minute disparities of sensation, as well as the power to make accurately graduated muscular response thereto." (James.)

SUMMARY OF THE PSYCHOLOGICAL ACTION OF ALCOHOL.

In presenting the following summary of the experimental work described in the preceding section, I would ask the reader to bear in mind that experimental psychology deals with very intricate problems; that many of its assumptions are still in dispute; and that here, as in other branches of science, numerous sources of error are encountered.

The psychological experiments thus far made appear to prove that moderate quantities of alcohol (15-30-45 grams) shorten the *simple* reaction time; the time required in a certain type of association process and in certain more elementary mental

efforts, such as reading in a whisper and adding columns of simple figures ; that is, processes in which central motor innervation is an important factor. This effect, that is, greater brevity of cerebral time, is tacitly assumed by investigators to indicate that the mental operations in question are performed with greater ease and with less friction ; an assumption for which there is no proof.

A greater tendency to premature and erroneous reactions is seen when the reactor has received alcohol. The reactor often believes that he is reacting more quickly than usual even when the cerebral time is longer.

In all those forms of reaction in which the reactor is required to dwell on or to compare sensations, alcohol causes a lengthening of the reaction time.

Larger quantities of alcohol than thirty grams, say the equivalent of a bottle of wine, lengthen the times of all the operations just enumerated ; and, in fact, depress every type of mental energy so far as psychologists have investigated the question.

In no respect is the action of alcohol in moderate quantities more striking than in its influence on the association of ideas. The time consumed in associations involving a subsumption judgment is, for example, only a little shorter than the normal ; but the time required to find a rhyme to a given word is considerably shortened ; and this state lasts for some time after the alcohol has been taken. Here it was noticed by Kraepelin that the associations seemed to run in the groove of custom ; that there was a greater increase in purely "outer" associations with no logical inter-connection. "Sound" associations were very frequent ; a proof that the association process tended rather to run into the region of stored concepts for sounds and movements than into other fields.

In Kraepelin's experiments the time required for the addition of columns of simple figures was found to be lengthened by even small quantities of alcohol, while in those of Partridge the time consumed in the association process in adding was found to be decreased.

In general, then, mental processes which involve the working up of conceptual material are not favored by moderate quantities of alcohol.

Experiments made on the effect of the continued daily administration of 40 to 80 grams of alcohol show a decrease after a few days in the ability to memorize and to add figures. This depression disappears rapidly on leaving off the alcohol. The continued administration of alcohol also changed the order of associations in experiments made to test this point, leading to a great increase in the number of the "outer" and "sensorily disconnected" forms.

As to the action of alcohol on the several senses, both special and general, it may be stated that the experimental work of the day proves conclusively that in any but very small quantities it has a sedative or depressant action. The so-called sense of effort which is brought into play in estimating differences between weights appears to be "stimulated" by small quantities (15 to 30 grams of alcohol), the result being that smaller differences between weights can be more accurately detected after alcohol than before.

Such quantities also stimulate muscular energy for a very brief period, which is followed, however, by a temporary period of depression.

The power to make "eye measurements," a function which is called into play in many of the arts and industries of life, is distinctly depressed when the individual takes a bottle of wine. Similar large quantities of alcohol diminish the acuteness of the senses of smell and touch. There are, unfortunately, no records to show how a single glass of wine or beer affects the cerebral functions involved in the operation of the senses just enumerated.

It will be seen that alcohol is not found by psychologists to increase the quantity or vigor of mental operations; in fact, it clearly tends to lessen the power of clear and consecutive reasoning. In many respects its action on the higher functions of the mind resembles that of fatigue of the brain; though with this action is associated a tendency to "greater motor energy and ease."

In speaking of a certain type of individual James says, "It is the absence of scruples, of consequences, of considerations, the extraordinary simplification of each moment's outlook, that gives to the explosive individual such motor energy and ease." This description aptly applies to the individual who is under

the influence of a "moderate" quantity of alcohol. It tends to turn the inhibitive type of mind into the "hair-trigger" type.¹ We have said that the speech and bearing of men, the play of their features, all bear witness to the action of alcohol on the brain; that it removes restraints, blunts too acute sensibilities, dispels sensations of fatigue, causes a certain type of ideas and mental images to follow each other with greater rapidity, and gives a "cerebral sense of richness."

Larger quantities, such as are for most individuals represented by one or two bottles of wine (ten per cent. of alcohol), may, according to the resistance and type of individual in question, cause a lack of control of the emotions; noticeably affect the power of attention, of clear judgment and reason; and decidedly lower the acuteness of the several senses. In many individuals such quantities will develop so marked an anæsthetic action that all the phenomena of intoxication may be seen to follow each other in due sequence, finally to end in the sleep of drunkenness.

There has been much discussion as to whether alcohol is in any sense a stimulant for the brain. We have seen that pharmacologists of high repute deny that it has this action; holding that alcohol is a sedative or narcotic substance which belongs to the same class as paraldehyde and chloroform; that its stimulating action is but fictitious; and that even the earlier phenomena of its action are to be referred to a paralyzing action on cerebral (inhibitory) functions. This theory assumes an unequal action on cerebral functions in the order of time. Kraepelin, however, holds that this is a purely subjective analysis; and that in the early stages of its action alcohol truly stimulates the motor functions of the brain; that a state of mental exhilaration, of "motor excitability," may coexist with undiminished power of perception and judgment. His psychological experiments on the action of alcohol, taken all in all, do not, however, entirely prove his position.

V. THE ACTION OF ALCOHOL ON MUSCULAR ACTIVITY.

In considering the relation of alcohol to physical labor a number of questions present themselves for solution.

Does it enable an individual whose food supply is sufficient

¹ This expressive term is borrowed from James.

for his needs to do more work? Does it enable the tired person to put forth new exertions? And if so, is it superior in this respect to tea, sugar, or other easily assimilable food products? Does the fact that alcohol is oxidized in the body, and that it therefore yields energy, make it a practicable food and store of energy for the muscles? Or is its utilization in this particular annulled by its psychic action, by its action in dilating the blood vessels of the body surface, etc.?

The statement is often made by those who are conversant with the affairs of practical life that even moderate indulgence in alcoholic beverages *during the day's work* diminishes the total amount of work done, and also affects injuriously the quality of that which is done. This statement is made in regard to the employees of railway and maritime companies, telegraphers, typesetters, bricklayers, scaffold builders, factory employees, etc. Even in such forms of activity as are involved in marching, in the work of the navy and digger, the regular though moderate use of alcohol during the day's work is stated to be without advantage, or even detrimental to the individual. This is mainly on account of its sedative action on the brain.

Taken in a broad way, these claims are correct.

Before recounting the experiments which bear on these subjects, we must inquire into the nature of fatigue. Physiologists have pointed out that the cause of fatigue after prolonged exertion is located in nerve cells to a larger extent than in the muscular apparatus itself; that nerve cells become exhausted (fatigued) before the muscles; and that the former also recover from fatigue more rapidly than the latter.

When a set of muscles has been exhausted by fatiguing, voluntary work until they longer refuse to obey the will, they may still be made to contract and to do considerable work if they be aroused by the direct application of an electric current. The fatigue of nerve cells that follows prolonged muscular exertion is supposed by some to be located in some of the lower centres of the cerebro-spinal axis; "perhaps in the cells of the spinal cord, upon the activity of which the transmission of the voluntary impulse depends." (Lombard.) Waller says: "In voluntary fatigue the degree of change is in decreasing ratio from centre to periphery. In other words, that the cell of higher function is relatively to the amount of effect which it

can produce more exhaustible than the cell which is subordinate to it in the cerebro-muscular chain."

Every one is familiar with the fact that the condition of over-training ("staleness") in athletes is a state of relative exhaustion of the central nervous system, and not of the muscles.

1. ACTION OF ALCOHOL ON THE MUSCLES THEMSELVES.

Gréhant and Quinquaud (1891) made a series of experiments on the dog which bear on this question, but only in cases of acute intoxication. The animal weighed 21.5 kilos, or about 43 pounds. The gastrocnemius muscle of the leg was used, its tendo Achillis being attached to a dynamometric myograph, which registered the amount of work done under a load or tension of from 270 to 371 grams. An electric stimulus of known intensity was employed to arouse the muscle to contractions; the one electrode being applied to the upper end of the superior tendon; the second to the lower end of the tendo Achillis. Alcohol of 25° Beaumé, that is, of about fifty-six per cent. by weight, was administered by the stomach in quantities of 100 grams and at intervals of a quarter of an hour; and the effect was studied on several series of muscular contractions after each injection or two of the alcohol. Under normal conditions, with a load of 300 grams, a muscular effort equal to 1700 to 2121 gram metres, with a load of 371 grams, one of 1700 to 2200 gram metres was registered for a certain number of contractions. After two injections of alcohol into the stomach the muscular effort amounted to only 1221 gram metres under a load of 300 grams. The ability of the muscle now fell off steadily with each new injection. After the fourth injection the work done with a load of 300 grams was only 921 gram metres, but rose in a second test to 1250 and again to 1400 gram metres. The final injection of 300 grams of alcohol of 28° Beaumé depressed the muscle so greatly that the work done under a load of 300 grams amounted to only 721 gram metres. At this time the animal was found to be completely drunk, a fact not to be wondered at when it is remembered that it had received about 350 grams of absolute alcohol, and that its blood at this time must have contained more than one per cent. of alcohol. The authors conclude that in acute poisoning with alcohol (the state of drunkenness) the muscular power is diminished to a very great degree.

It is to be regretted that tests were not made with smaller quantities of alcohol, such as correspond to its moderate use by human beings. We are at present in ignorance how alcohol, in quantities which have no very marked mental effect, acts on the muscular apparatus itself, considered apart from the central nervous system. As already pointed out, we must accept the fact that alcohol, like many other compounds containing carbon, hydrogen, and oxygen, is oxidized in the muscles and elsewhere, and therefore yields energy. But we do not know whether the muscle cell finds it a difficult task to oxidize the alcohol even in small amounts; or whether the alcohol interferes in any way with the taking up of nutritive material or with the removal of irritating fatigue products from the muscle cell. We know that methyl alcohol is never oxidized in the body without leaving an irritating residue in the shape of formic acid. To hold that ethyl alcohol is oxidized in the body to carbon dioxide and water without the appearance of any intermediate products is not only opposed to chemical theory, but also to the experimental evidence in hand. Only recently Thomas has shown that the blood of rabbits intoxicated with ethyl alcohol contains a volatile fatty acid whose nature was not determined, but there can be little doubt that it was acetic acid. The alkalinity of the blood was sometimes lowered to one half the normal alkalinity, and the carbonic acid content was also much diminished, this acid having been displaced by the volatile fatty acid arising in the course of the oxidation of the alcohol. When alcohol is consumed in moderate quantities the immediate oxidation product just referred to probably exerts no harmful action, as it is itself soon oxidized to a carbonate. It is nevertheless possible that here will be found, in part at least, an explanation of the fact that alcohol is not found to be as practicable a source of energy for prolonged physical labor as equivalent amounts of foods proper. In this connection, too, we may take note of the very recent investigation of Singer, who has shown that in the rabbit alcohol causes an increased amount of oxygen to be taken up, and that this is due in part to an increase in the motor activity of the digestive tract, but still more to the need of the organism for an increased combustion and an increase of energy which shall compensate for the heat lost from the body in consequence of the vascular dilatation caused by the alcohol.

For this animal, at least, alcohol would constitute but a poor source of muscular energy, for its mere presence when the animal is at rest causes a greater need of oxygen, a need which is further increased by any work which may be imposed upon the muscles. The need for oxygen is therefore greater than it would be in case some substance, such as starch, were supplied as a source of energy.

Kobert, in 1882, made a few experiments on frogs which bear on the question in hand. The hind legs of the frog were attached to a registering apparatus (*Arbeitssammler*) which indicated the extent of the individual contractions and also enabled the work to be calculated. As in the experiments of Gréhant and Quinquand, an electric stimulus was used, but this was applied to the skin of the uninjured animal. Large doses of alcohol, that is, thirty milligrammes properly diluted, had a temporary depressing effect on the amount of work done. Small and average doses somewhat increased the amount of work done by four frogs and lowered it in two others. Kobert does not, for reasons which cannot be taken up here, consider it as at all proved that the muscles are enabled to do *more* work after alcohol, but believes that he has shown that small and average doses do not affect them in any deleterious manner. At present, then, we have no experimental grounds for believing that small or very moderate quantities of alcohol exercise any beneficial direct action on the muscles of men and warm-blooded animals, though future experiments may show this to be the case. Large quantities of alcohol, however, as we have seen, lower the ability of the muscles to do work in response to an external as distinguished from a voluntary stimulus; much alcohol in the blood causes a decline of muscular energy by a direct action of some kind on the muscle itself.

Further reference to this question of the direct action of alcohol on the muscles themselves will be made in the succeeding section, in which the work of those who have employed the ergograph is reviewed.

2. ACTION OF ALCOHOL ON VOLUNTARY MUSCULAR EFFORTS.

Much experimental work has been done on the influence of alcohol on voluntary work. So far as this work has been done in laboratories it has not concerned itself with labor performed

according to the usual acceptance of the term; that is, to such operations as marching, digging, the work of the navy, etc.; — but rather with the employment of certain groups of muscles, either of the whole hand, or more often, of the flexors of a single finger. The apparatus used was sometimes a dynamometer, and in recent years the ergograph of Mosso. This latter instrument enables the experimenter to calculate with great accuracy the amount of work done in a given time by one of his fingers, which is fitted with a collar of leather attached in its turn to a weight whose movements are properly registered by a recording slider on a revolving drum. The muscles of the finger are contracted every few seconds, the weight being lifted each time as high as possible and then immediately lowered; and this is kept up until exhaustion occurs. After a brief interval of rest contractions can again be made. In this way series of graphic records may be obtained, and the influence of drugs, food, etc., on the work done may be studied.

The results of numerous experiments are not entirely concordant; but, as we shall see, the majority of experimenters have come to the conclusion that small quantities of alcohol have but a slight and temporary stimulating action on voluntary work; and all are agreed that any considerable quantity, say two ounces of absolute alcohol (the amount usually assumed to be oxidized in twenty-four hours, with only the usual physiological loss by escape through the excretory channels), lowers the ability to do muscular work. In numerous dynamometer trials made by Dehio and Kraepelin on themselves the following results were obtained. In Dehio's case, thirty grams of alcohol (about ten ounces of wine, with ten per cent. alcohol) regularly caused a diminution of muscular power usually lasting at least half an hour. The dynamometer would register, for example, before alcohol on the average from 102 to 104; after alcohol the averages would run from 92 to 95.

In Kraepelin's case, twenty grams of absolute alcohol caused as regularly noticeable improvement in the ability to squeeze the dynamometer. Thus, on the normal day the instrument registered averages ranging from 91 to 97; on the day when alcohol was used the averages ranged from 96 to 104. As in Dehio's case, each of these averages represents the "probable average" as calculated from a series of twenty-five trials with

the instrument. This increased ability on Kraepelin's part to expend muscular energy lasted but a short time after taking the alcohol, sometimes less than ten minutes; and soon gave place to a temporary depression of muscular ability.

De Sarlo and Bernardini corroborate Kraepelin's observations, and find that seventy grams of rum cause a very temporary and slight increase in muscular power.

The ergograph, as used by modern investigators, is an instrument better adapted for such studies. Unfortunately, however, even in the latest experiments on alcohol with this instrument, sufficient care has not been taken to eliminate sources of error. In similar work on the influence of sugar, proteids, etc., on the voluntary muscular work, Schumberg, Fraentzel, and others have found it necessary to keep all the apparatus, except the finger strap and the string leading to the weight, concealed from the subject of the experiment. The taste of the alcohol, too, should be disguised, and "control" tests with similar tasting fluids containing no alcohol should be made. These precautions should be taken in order that psychical influences, inimical to the course of the experiment, may, as far as possible, be eliminated. The experiments with the ergograph now to be cited are all vitiated more or less by the fact that these precautions were not taken.

Lombard has used the ergograph in a few experiments on the effect of alcohol on his own voluntary power. In one experiment, alcohol in the form of an ounce of whiskey was taken at 11.30 A. M., with the result of increasing the muscular power threefold *thirty-five minutes* after.

In a second experiment with an ounce of whiskey, Lombard found that "the alcohol greatly increased the power to do voluntary muscular work, in spite of the fact that the strength of the muscle, as determined by its response to electrical stimuli, was not greater. Though the nerves were not studied in this case, the effect of the alcohol to increase endurance without doubt can be referred to its action on the central nervous system." The results of this second experiment with whiskey are stated in the following form: —

	Work done by fifty voluntary contractions.	Work done by fifty contractions excited by electricity.
Before alcohol . . .	27.0 kgm.	22.8 kgm.
After alcohol . . .	43.4 kgm. (nineteen minutes after the whiskey had been taken).	18.4 “

Two other experiments are cited, in the first of which one glass of claret taken with dinner was found “shortly after, to make the strength greater at 8.15 P. M. than at 10.10 P. M., the time of the usual evening maximum of the power.” In the second of the experiments with claret, one glass was taken with lunch at 2.20 P. M., and a second glass was taken at 2.50. The tests were made at 4.15 P. M., with the result that “the strength at 4.15 P. M., the time of the usual afternoon minimum, was greater than at 10 A. M. or 10 P. M., the time that the strength is usually most. The strengthening effect began to be felt within a few minutes, and lasted in one case an hour and a half.” Lombard regards it as possible that “the primary strengthening influence would have been followed by depressing after effects,” had larger quantities of alcohol been taken.

Kraepelin, in referring to Lombard’s work, denies the possibility of the long continuance of the beneficial after effect.

H. Frey (1897) has made a large number of experiments, both on himself and others, with Mosso’s ergograph, and his results have led to much controversy. The effects of a large number of alcoholic beverages, such as cognac, rum, wine, beer, etc., and also of pure alcohol, were studied. The quantities consumed were always small, as, for example, 10 c. c. or one third ounce of cognac, one and one half to two and one half decilitres of wine or beer.

Frey concluded that the effect of such small quantities was dependent on the condition of the muscle. If the muscles of the finger were not in the least fatigued, the alcohol served only to lower the height of the individual contractions; the muscle was less efficient after alcohol than before. In case, however, the muscles in question were first fatigued by a series of contractions, the alcohol had a stimulating action, and enabled the

working finger to raise the weight to a higher level than when no alcohol was given, though never to the height to which the unexhausted muscle could raise the weight. This stimulating action of alcoholic beverages was experienced inside of one or two minutes after their consumption.

In explanation of this action of alcohol, depressant for the non-fatigued and stimulant for the fatigued muscle, Frey offers the following explanation: Alcohol has a double action; it has a paralyzing action on both the central and the peripheral nervous system; and it also serves as a source of energy for the muscles by virtue of its nutritive qualities. In the unfatigued state the muscles find in the blood all the nutritive material that they can make use of; and alcohol can only exert its sedative or paralyzing action on the nervous apparatus, the result being that less work is accomplished. When the muscle is fatigued, however, the alcohol supplied to the blood acts as a new source of energy; its good effect in this direction overbalancing any evil effect exerted by it on the nervous system; and the result is an increase in the amount of work done.

In proof of the fact that alcohol acts on the fatigued muscle in the manner described, curves and experiments are given in which the effect of alcohol on the fatigued muscle is shown when its contractions are aroused, not by the will but by the direct application of the electric current to the muscle. In this case also the fatigued muscle performed more work.

A similar experiment bearing on this last point, made by Lombard with whiskey, and which has already been cited, had the opposite result. The work done by fifty contractions was, before alcohol, 22.8 kilogrammetres; after alcohol, the work done by fifty contractions was only 18.4 kilogrammetres. As Lombard made but the one experiment, we cannot consider this evidence as conclusive for the point at issue.

It will be seen presently that Frey's results are no doubt correct, in so far as the effect of alcohol on the fatigued muscle is concerned. Destrée, as we shall see, corroborates him on this point; but shows that the non-fatigued muscle is affected in exactly the same way by alcohol.

Frey's plausible explanation of the action of alcohol on the fatigued muscle will not stand criticism. Fick has pointed out that when the flexor muscle of the finger has been employed

until it is fatigued, that is, until the individual can contract it only feebly, it is impossible that the blood should lack nutriment for the muscle in question. The work done by the finger when exhaustion becomes evident has amounted to about four kilogrammetres. Now, the minute quantity of eight milligrams of sugar would suffice to furnish the muscle with the energy needed for the accomplishment of this amount of work. The consumption of this small amount of sugar would lower the percentage of sugar in the blood from 1.3 per cent. to 1.298 per cent., a diminution so slight that it is evident that the blood, passing through the muscle, is still richly supplied with energy-yielding material. This is the more certain when it is borne in mind how many other energy-yielding substances, such as glycogen, proteids, etc., are at the disposal of the muscle.

Frey has neglected to take into account the fact that fatigue is more largely a question of the nervous than of the muscular apparatus; and that the explanation of the action of alcohol in stimulating a fatigued person to renewed exertions must be sought in its action on the nervous system. Frey does not, however, deny that alcohol has a mental influence on fatigued persons, but states distinctly that it lessens the sensation of fatigue.

The next work of importance on this subject is the investigation of E. Destrée (1898). This author's results and conclusions are in accord with those of Kraepelin, Lombard, and others, and also with the experiences of practical life. His apparatus and the details of his method are like those of Frey. The work of the flexors of one finger is similarly expressed in kilogrammetres, and similar graphic records are furnished. Destrée shows that Frey failed to note the stimulating action of alcohol in his experiments on the non-fatigued muscle, because he did not make his tests soon after the administration of the alcohol; but only at a time when the depressant action of the alcohol had already become evident.

The results arrived at in this research are as follows:—

1. That alcohol has a favorable action on the performance of muscular work, both when the muscles are vigorous and when they are exhausted.
2. This favorable and stimulating action is seen almost immediately after the administration of the alcohol, but lasts only a very short time.

3. A paralyzing action always succeeds the stimulation. In about half an hour after the administration of the alcohol the work done reaches a minimum ; and fresh doses of alcohol show only a slight stimulating action.

4. This later paralyzing action of alcohol overbalances the primary stimulating effect in such a way that the sum total of the amount of work done with alcohol is less than that done without it.

5. Similar depressing effects are not seen to follow the use of tea, coffee, or kola.

Very recently Schumberg, whose previous careful work with the ergograph under the direction of Professor Zuntz of Berlin affords a guarantee for the trustworthiness of his present research, has compared the action of alcohol on muscular labor with the similar effects of such agents as tea and coffee. His conclusions are expressed about as follows : that alcohol does not appear to be a food stuff like the carbohydrates, which by their oxidation in the body are able to act as a source of energy for work. It is rather to be classed with excitants such as coffee, tea, extract of kola, etc., which act as stimulants for the muscles only when a sufficient supply of nutrient material is circulating in the blood.

Schumberg found that when the body was first fatigued by hard labor at a lathe, a small dose of alcohol (10 c. c.) was powerless to cause an increase in muscular work, while in the unfatigued state of the individual, when much easily oxidizable nutritive material was circulating through his muscles, the same quantity of alcohol caused a decided but only temporary increase in the work done.

According to Schumberg, then, alcohol is devoid of a direct dynamogenic power for muscular tissue.

It will be seen that Schumberg's investigations are of especial value because they were carried out on another individual, thus eliminating a personal element of error, and also because he did not content himself with fatiguing merely that particular group of muscles used in the ergograph experiments, but effected the exhaustion of easily oxidizable material in the blood by employing the whole body in the performance of hard labor.

More recently still Scheffer, unaware of Schumberg's work, has taken up this subject in a careful manner. This author

detects the vulnerable points in the work of Frey and others, and also criticises certain points in the technique of Destrée. He demands that long series of comparable experiments be performed, that the well-known influence of practice shall fall equally on the series of trials performed with and without alcohol, that the groups of muscles which are used to operate the ergograph be really non-fatigued, and that due credit be given to the psychic factor in experiments of this nature. The author himself serves as the subject of the ergographic experiments described by him. It may be remarked in passing that he describes himself as one who takes wine or spirits under exceptional circumstances only, but that he usually takes a glass of beer with his afternoon meal. Without further detail it may be stated that his numerous ergograph experiments lead the author to declare that moderate doses of alcohol (10 grams with 90 c. c. of water) cause an immediate and temporary increase in voluntary muscular work, followed by a decrease to a point below the normal.

If the particular groups of muscles employed are first fatigued, the stimulating action of the alcohol is still more apparent. These results were obtained in three series of experiments, in the first of which the tests were begun immediately after taking the alcohol; in the second fifteen minutes after the alcohol was taken. In the third series of tests the alcohol was taken thirty minutes before the experiments were begun, and in this series the mechanical labor performed was 5.61 per cent. less in amount than in the experiments without alcohol. In the first series there was a gain of 5.81 per cent. in the work done as estimated in kilogrammetres, in the second series the gain amounted to 8.7 per cent. The results of the third series show very clearly how rapidly the fatiguing effects of alcohol come on, and how much they tend to repress the output of energy by the muscle substance.

Scheffer also gives the results of a series of careful experiments on frogs, which show that after the elimination of the action of the peripheral ends of the motor nerves by means of curare, no effect whatever can be obtained by the use of what may be described as moderate doses of alcohol. When no curare was used, an unmistakable increase in the work done always followed the administration of alcohol. Scheffer there-

fore concludes, as Schumberg has done, that alcohol cannot act as a dynamogenic substance for muscle tissue.

Scheffer, as we have just seen, finds that alcohol can only cause an increase in the work done by a muscle when there is present a sufficiency of nutritive material, and he appears to incline to the view that its influence lies in its power to cause a greater taking-up of nutriment, though whether he has the digestive tract or the muscle cell itself in mind, it is impossible to say.

Scheffer also raises the question as to how alcohol acts as a temporary stimulant for the muscles when they are employed in voluntary efforts, even though it does not itself serve as direct source of this energy, and he falls back on the assumption that the primary increase as well as the later depression in muscular work find their best explanation in an increase in the irritability of motor nerve fibres and motor end plates, which is soon followed by a decrease in excitability. That alcohol first increases and then rapidly decreases the electrical excitability of motor nerves is known from the work of Waller, of Gad and his pupils, and of Werigo.

Plausible as this hypothesis seems, it needs further proof for its acceptance, for we know too little at present of the relation that exists between voluntary use of the muscles and their irritability and conductivity. It would seem that the well-known action of alcohol itself and of the intermediate products of its oxidation on the central nervous system would also have to be taken into consideration by any theory which seeks to explain how alcohol produces the temporary increase of muscular energy just referred to.

Partridge has also given some results of experiments on the effect of alcohol on physical work with the ergograph.

The instrument used by this investigator was the hand dynamometer of Salter, and the tests were made chiefly on himself, though one other subject (H) was also employed. The results obtained are summarized in the following words: "The effect upon subject H of six grams of 33 $\frac{1}{3}$ per cent. alcohol taken just before work began was to decrease decidedly the working power. Forty-five grams did not affect the amount of work done by subject P, but a comparison of the curves for normal and alcohol days indicate that alcohol produced a slight but steadily progressive stimulating effect."

Ninety grams also failed to affect the total amount of work done by P, but in this case the effect is clear in an alteration of the work curve. There is an increase of work done during the first half hour on the alcohol days and a decrease during the second half hour.

The effect of ninety grams upon the work done during the second hour after the alcohol was taken was to decrease the amount, which was less for each period during the hour.

If we sum up the results of the experiments just described, we find them to be in admirable accord with the opinion so often expressed by large employers of labor, by army officials, explorers, and athletes, that alcohol does not give any persistent increase of muscular power, but only enables a brief spurt to be made, which is soon followed by a depression of energy to below the normal.

According to Schumberg even this primary, greater liberation of energy will not be effected by alcohol if the muscle tissues themselves are not at the time richly supplied with nutritive material.

All of the more carefully conducted experiments make it appear probable that alcohol does not act directly as a force-yielding substance to muscle tissue, but acts rather in the manner of agents whose primary action is upon the nervous mechanisms, either central or peripheral, which are concerned in voluntary efforts. Such an explanation as to the manner in which alcohol acts should not, however, be accepted too hastily. Even though we cannot furnish proof with the ergograph that this oxidizable drug yields energy which is utilizable by the muscles, it must be borne in mind that it is possible that the energy liberated in muscular tissues during the oxidation of alcohol is in reality utilized, but that concomitant occurrences nullify the full utilization of this energy. In other words, the algebraic sum of all of the effects of alcohol on muscular tissue bears a minus sign as compared with the sum of the effects in the case of starch, sugar, fats, and proteids. In the first quarter of an hour or so, especially under the right conditions of nutrition, this algebraic sum of the effects of alcohol would have a positive sign. That coffee and tea also stimulate the muscle apparatus in voluntary work does not in reality put these substances and alcohol in the same class. The chemical

and physico-chemical occurrences in muscle and nerves may differ widely, and yet the results as expressed in work may be of the same order.

The following considerations make it appear probable that even in the case of the non-harmful muscle foods, the increase of muscular energy which *immediately* follows their ingestion does not have its origin, at the very first at least, in the oxidation of these foods in the muscles.

Experiments with the ergograph similar to those just described have been made in recent years, in which the effect of sugar, proteids, etc., on voluntary muscular work has been studied. These experiments have shown that these easily absorbed foods have an immediate effect on the exhausted muscle, stimulating it to the performance of more work. The influence of mental suggestion, of the belief in the efficacy of the thing taken into the stomach, has been pretty well excluded in the latest of these experiments. It has also been shown that the nutritive action of the sugar or proteid taken is perhaps not the chief factor in the *immediate* increase of strength which it causes. It is well known that the alkalinity of the muscle decreases with the amount of labor performed, and that "fatigue products" accumulate. Now the introduction of foods and stimulants into the stomach increases the flow of the gastric juice; and as a consequence the alkalinity of the blood is increased. In this way, as Fraentzel has pointed out, the diminished alkalinity of the fatigued muscles may be raised to a more normal state, and the muscle may again be aroused by voluntary impulses. Fraentzel has shown that a few grams of sodium bicarbonate given by the mouth have a restorative action about equal to that of thirty grams of sugar; but not equal to that of a like amount of albumen.

Purely chemical and physico-chemical, as well as physiological considerations must, therefore, enter into the discussion of the complex question as to how alcohol affects physical working power; and these considerations must also be borne in mind in a discussion of the nature of central and peripheral fatigue. Both science and empiricism teach that alcohol is not a practicable source of energy in the performance of physical labor.

The experiments of Aschaffenburg may be cited to show the influence of alcoholic beverages on the efficiency of men engaged

in a pursuit which involves little muscular effort of the kind just described, but rather an accurate muscular response to mental performances. Working under Kraepelin's direction, this investigator has recently (1896) published an investigation entitled "Practical Work and Alcohol," in which he gives an account of the action of alcohol as affecting the work of a number of typesetters. These experiments were made in accordance with the rules of physiological psychology on four Heidelberg typesetters who had volunteered to serve as the subjects of them. These men were respectively 42, 36, 25, and 23 years old; and even the youngest had been engaged in his trade for nine years. The oldest of the party was accustomed to take four glasses of beer a day, except on Sunday, when he consumed from eight to ten glasses; the second took one or two glasses on week days and four to five on Sunday; the third took none on week days and two to three glasses on Sunday; the fourth took three glasses a day during the week and five to six glasses on Sunday. All stated that on Monday their work was less easily performed, and that they made more mistakes. No. 3 felt dull and languid, and No. 1 complained of headache, dizziness, and sleepiness, and often had all the symptoms of a man who had been on a "spree" the day before.

In order to secure "normal" days for tests, that is, days on which the experiments were to be made without alcohol, the men were required to abstain entirely from alcoholic beverages for the twenty-four hours preceding. The tests, both with and without alcohol, were made at the same hour each day; the men worked in their usual places in the printing establishment, and used type with which they were thoroughly familiar; and instead of a written manuscript, printed material was used as "copy." In short, the experiments were so arranged as to constitute the sort of test required in practical life, and yet meet the requirements of laboratory exactness. It is evident that both the quantity and the quality of the work done by the men could be estimated.

Four days were used for the tests, the first and third of which were "normal" days; the second and fourth were "alcohol days." On the alcohol days each man received 200 grams (nearly 7 oz.) of a Greek wine, Achaja, containing about eighteen per cent. of alcohol, a quarter of an hour before the

trials took place. Without taking up the experiments in detail, we may give Aschaffenberg's conclusions as follows :—

1. The alcohol given caused no change in the quality of the work, as compared with that of the days when no alcohol was given. Very few mistakes were made. Kraepelin and Fürer have shown that alcohol tends to cause the "reactor" to respond prematurely, and to make "erroneous" reactions (*fehl Reactionen*). In the case of these typesetters, nothing of this kind was seen.

Only on Mondays, after the Sunday indulgence, did their work, according to their own accounts, show a greater percentage of errors and give evidence of premature and "erroneous" reactions.

2. The alcohol taken (thirty-six to forty grams of absolute alcohol) diminished the *amount* of work done. Among the eight trials there was but one in which the amount of type set was not below that of the normal days. Assuming that fatigue and practice had no influence on the result, the diminution in "output" amounted to fifteen per cent. of the expected or calculated output. The effect of fatigue alone was estimated to lower the output by only 6.5 per cent, as compared with what was normally to be expected. Even if the assumption is made that fatigue lowered the output of the alcohol days, there still remains a considerable deficit, which can only be attributed to the retarding action of alcohol.

Experiments of this nature in other fields of industry would be of great value if made by competent psychologists.

VI. SOCIOLOGICAL CONSIDERATIONS.

After the review of such work as has been done by experimenters on the action of alcohol, a number of questions still present themselves.

First: Is there a "moderate" quantity of alcohol for the average adult,—that is, a quantity to whose habitual use no bad results of any kind can be traced?

Second: What benefit is derived from this moderate quantity, and in what cases is its use permissible?

I have incidentally given expression to the opinion that alcohol is not a practicable food in the sense in which fats and carbohydrates are foods. Its dietetic value in medical practice, as

Ewart remarks, "resides less in its nutritive coefficient than in its beneficial effect upon the digestive and nervous functions."

I also hold that it is not of dynamogenic value for muscle tissue, that when all the facts are summed up it may be defined as an easily oxidizable drug with numerous untoward effects which inevitably appear when a certain minimum dose is exceeded. For all practical purposes, science and empiricism unite in classing it with the more or less dangerous stimulants and narcotics, such as hasheesh, tobacco, etc., rather than with truly sustaining foodstuffs.

That there is a "moderate" or average permissible quantity of alcohol I conclude from the results of experiments already cited; from the opinions of medical authorities in many fields; from the writings of economists, explorers, and military authorities; and lastly from my own observations during a long residence in European countries; and this "moderate" quantity I believe to be represented by one, or at most two glasses of wine (ten per cent. alcohol) or one pint of beer, or their equivalents in terms of alcohol, in the twenty-four hours.

That this quantity is far below what has been proved to be capable of oxidation in the body in that time, and far below what is tolerated by some individuals, is not to the point; since the mean oxidizable amount can be shown to have various untoward effects, oxidizability cannot be made the measure of usefulness in regard to this substance; and to the objection that this amount is so small that it amounts, practically speaking, to teetotalism, we can only say that it is for the user to decide whether the benefits claimed for it actually obtain in his case. Both medical science and practical experience have placed such restrictions on the use of alcohol in respect to age, condition of the person, employment, and mode of life, time of day when taken, etc., that it becomes more and more apparent that the quantity habitually taken must be *very small* for the average adult, if he would avoid all evil effects.

It is often assumed that a substance which is ordinarily called a poison must have, even in the smallest quantity, an injurious effect; that the action of the smaller, and to all appearances non-toxic quantity differs not at all in *kind*, but in *degree* only, from that of the large dose; that its action is simply weaker in proportion to the decrease in dose.

Such a proposition can only be made in this unrestricted manner by those who fail to reflect on the great complexity of the animal organism, and who are ignorant of the fact that gradual changes in the amount of the poison administered cause varying changes in the symptoms in proportion as this or that organ, this or that tissue, this or that constituent of the body is affected by its own sufficient quantity of the poison.

In speaking of the influence of stimulants and narcotics on mental states, Bain has well said : " In organic influences you are not at liberty to lay down the law of concomitant variations without exception, or to affirm that what is bad in large quantities is simply less bad when the quantity is small. There may be proportions not only innocuous but beneficial."

We have seen that at least one third of an ounce of alcohol must be taken before the experimenter can detect even the most insignificant departure from the normal course of brain and nerve processes. Similar and even larger doses are required to produce such occurrences as flushing of the skin or increased rapidity of the pulse or respiration. In order to cause even a slight increase in the intake of oxygen, two thirds to one ounce, or the equivalent of seven to ten ounces of an ordinary table wine, are required. The effects vary with the dose, and it remains to be shown that harm is done when the dose is less than that required in psychological and physiological tests.

As far as we possess knowledge of the effects of any given poison, we can always speak in physiological terms, at least, of the different *kinds* of action developed by different doses of the poison, as well as of differences of *degree* of action. For instance, *nux vomica* contains the deadly alkaloid strychnine, which, in a certain dose, causes frightful convulsions of all the muscles of the body. Laboratory experimenters are, however, well acquainted with the fact that this period of convulsions can be tided over, with the help of vigorous artificial respiration ; and that gradually larger doses of the poison can be injected, until finally a period of relaxation is attained, in which the heart still beats, and life continues for a number of hours, provided that artificial respiration be maintained. Let the artificial respiration be discontinued, the animal dies without making a movement ; all reflex activity is annihilated, convulsions are impossible, and a new and unsuspected kind of action

has developed. The strychnine has now developed quite new symptoms ; it has paralyzed certain regions of the central nervous system, and has also paralyzed the motor end plates, or joining places of the motor nerves and muscles, so that the animal would be unable to move its limbs even if it could will to do so. Strychnine has, in this larger dose, now developed a true curare action, or arrow poison action, unknown to the ordinary toxic dose.

Similarly, arsenic and mercury, which in large doses are powerful irritants of the gastro-intestinal tract, are daily administered in medical practice in small doses ; and in such a way that no trace of this kind of action is apparent ; but only a deep-seated and obscure chemical action takes place, affecting the nutrition of the body.

That these differences in respect to the *kind* of action are possible is owing to the physical and chemical constitution of the body ; and also in some instances partly to the fact that many poisons develop different physical and chemical properties according to their degree of dilution in a given medium. Neither toxicology nor pharmacology, therefore, lends any support to the assumption that we have just considered.

We may here repeat a statement made in an earlier section of this paper, namely : that, without exception, all poisons are capable of being taken without *demonstrable* injury in a certain quantity ; which is for each of them a special, though sometimes very minute, fraction of their toxic or fatal dose. There is no substance which is always and everywhere a poison. The term is relative ; conditions and circumstances of various kinds must always enter into the conception of the term. No one would maintain, for example, that a cup of delicately flavored tea is in any sense injurious or poisonous to the average healthy adult. And yet caffeine, the active principle of this cup of tea, is a poison as surely as is alcohol.

It might be replied that in these and similar instances *some* degree of the toxic or injurious action of the poison is surely present ; although not to be detected by methods in present use.

If all substances known to be injurious in large doses are to be entirely given up on the unproved assumption that small doses are also injurious, then all condiments and spices must be removed from our tables. Even sugar in concentrated solu-

tion is a powerful cell poison. It is not probable that even an increasing refinement of experimental methods will ever establish the truth of the proposition that what is harmful in large quantities must still have some of this quality when the dose is small. That there is no natural law of this sort is proved by the fact that certain poisons are normally present in our tissues in such quantities that they subserve no harmful but rather a beneficial purpose. They appear, indeed, to be absolutely essential to the continuance of life. Such are the active principles of the thyroid gland and of the suprarenal capsules, both of which are far more powerful poisons than alcohol, that is, their lethal dose is several hundred times smaller. Then, too, our tissues are constantly bathed by fluids in which numerous poisons are contained whose percentage strength in health falls below the poison line. When their excretion from the body or their oxidation is prevented, their highly poisonous properties at once become manifest.

There are good grounds for believing that alcohol itself is always produced in very minute quantities in the course of bacterial fermentation in the intestinal canal, that it is, in fact, normally present in the healthy organism.

We now return to the special question as to whether alcohol may be introduced into the body in doses having a certain physiological and yet non-harmful action. We have seen that these terms are relative. We know that living organisms in general are endowed to a certain degree with defensive powers; not only against poisons which are inseparable from their very constitution, but also against those which are introduced from without, either by chance or design. To repeat, it has been demonstrated that continuance of life and good health are compatible with the presence of certain poisons in small quantities in the blood, and old age is attained in spite of them; although we are in ignorance as to what relation, if any, exists between these poisons and the longevity of the average normal individual.

As to the experience of mankind, it has shown that in wine-drinking lands thousands of people have taken wine in great moderation all their lives, without having *demonstrably* shortened their days or in any way affected health and strength.

The distinguished German physiologist, Professor Fick, who

late in life became a total abstainer, says, "There are certainly many people who are absolutely uninjured by a daily moderate consumption of alcohol."

The little alcohol taken by such individuals is oxidized and otherwise taken care of; just as is the case with a large number of poisonous and non-poisonous substances already referred to as circulating in the blood. These moderate quantities of alcohol are sufficient to gratify the individual's desire for a sedative or "mental stimulant," for a stomachic, or for an adjunct to social life; and when the quantity is not more, say, than a glass of wine a day, we may accept it as nearly demonstrated as such a proposition can be, that life is not shortened thereby, and that no toxic action resulting in any form of ill health is developed.

From the experiences of Greely, Stanley, Blessing, and others, instances of the occasional beneficial action of alcoholics may be gathered, which further bear out the assertion that they are not a poison in small doses; and which also forcibly illustrate the mental action of alcohol.

Greely says, "The use of rum in our home quarters at irregular intervals served an excellent purpose in stimulating the mental faculties; which, in the case of some of the men, seemed to be deadened and sluggish, owing to the monotonous character of our surroundings and to the unvarying routine of duty. During our two years' service at Conger, I did not drink in all a pint of spirits, though occasionally I took a glass of light wine; and my own experience was, that I was as well without alcohol as with it, though the social effect of wine among the officers was undoubtedly good." And again, "During the boat retreat southward from Conger to Cape Sabine, in August and September, 1884, a considerable quantity of rum and whiskey was taken with the party; but, although there was much exposure from great physical labor, more than half of the journey was completed before the issue of the spirits was begun. It was commenced at a time when the party was somewhat disheartened by the surroundings; and the particular result then sought was to benefit the men mentally, rather than physically. The use of rum during the boat retreat appeared to be most beneficial when given to the men just after the day's work was over, and after they had entered their sleeping-bags. Before

reaction came the men received hot food. Every one who could avoided drinking the rum until he had entered his bag. The men always expressed most strongly their appreciation of rum and its effects after a day spent in exhausting labors, under discouraging circumstances, and with unfortunate results; so that I judged the effect to be a mental stimulant and benefit, rather than a physical one. In addition to the effect upon the mind, it produced in the chilled, damp, and half frozen men a marked feeling of warmth, which, in my own case, appeared to result from an increased surface circulation; and in addition, the alcohol evidently had narcotic properties, for it speedily induced drowsiness and greatly promoted sleep. These special issues of rum, either in the field or during the retreat, rarely exceeded half a gill at a time; and when the men received for urgent reasons or on particular occasions double the amount, they stated to me that its beneficial result seemed to be little if any greater than that of half of a gill. The subject of alcohol was frequently and generally discussed during the winter at Cape Sabine; and all, without exception, concurred in the opinion that spirits should be taken after a day's labor was over, and not before or during exhausting work, nor while suffering from exposure which was to be continued."

Stanley is chary of recommending alcohol at all in the tropics; and says, "In the tropics I advise no one during the hours of daylight to touch liquor, unless a medical man prescribes a certain quantity to be taken, when it is absolutely necessary; that wine — a good red or white wine — should be taken only after sunset at dinner; half a pint, watered if more agreeable, is what I consider as a moderate quantity, that may be safely taken as soothing to the nerves and provoking early sleep. After a full night's rest one will rise with a clear head, clean tongue, and can as easily do a full day's work in the tropics as he can in temperate latitudes."

Dr. Blessing, the able physician who accompanied Nansen's expedition, says of the use of alcohol in polar expeditions, "Fully convinced as I am that alcoholic drinks are an unnecessary and perhaps dangerous addition to the weight of a sledding outfit, I must still hold that a moderate quantity is in place in times of festivity for those who must remain inactive in winter quarters. The heavy requirements on the system made by

bodily exertion forbid the use of stimulants ; but monotony of life, and the absolute lack of new and diverting impressions, make its use very desirable. It can do no harm to rouse the mind and courage by help of a glass of wine." During the following tedious winter, the crew had recourse on rare occasions of festivity, as holidays and birthdays, to some of their national drinks, and with only the best effects.

We have seen that increasing knowledge as to the true action of alcohol has placed numerous restrictions on its use ; that all of these restrictions point rather to the wisdom of the occasional than to its habitual use.

Laboratory experiments, like some of those described by Kraepelin, and made on a special and trained class of individuals, may prove that it has a temporary stimulating action for certain of the simpler mental functions ; but no one should attempt to deduce from these experiments any rules for the practical use of alcohol as a brain stimulant. These experiments have a value, simply in elucidating for critical minds the details of the action of alcohol on the brain. In the operations of daily life, however, the mind is called into play in many ways ; nowhere in the affairs of men is a single and elementary type of mental operation the rule. We have seen that alcohol from the very first has a depressant action for higher mental functions. Hence it is, that in all those avocations of life where keen senses, sharp attention, the ready and immediate action of a clear judgment, or great concentration of the mind are called for, alcohol in any form or amount is injurious when taken *during the performance of the duty in hand*. He who has mental labor of an exacting kind to perform, and he upon whom great responsibilities devolve, is forced, if he would be at his best, to use alcohol as a restorative agent only at the proper season ; he must behave to it as he does to many other pleasures and luxuries in his environment.

Both science and the experience of life have exploded the pernicious theory that alcohol gives any persistent increase of muscular power. The disappearance of this universal error will greatly reduce the consumption of alcohol among laboring men. It is well understood by all who control armies or large bodies of men engaged in physical labor, that alcohol and effective work are incompatible. That part of the race which

has work to do will, perhaps, some day accept the principle of the very moderate use of alcohol at the *proper time and place*, as the only principle compatible with its non-harmfulness, or with possible benefits to be derived from it.

We have seen that the action of alcohol on the brain is the prime cause of its consumption ; its taste and odor, its "stimulating" action for the digestive tract, the circulation, etc., are all in themselves minor considerations, although they enter into the conception of the value attributed by mankind to the various forms of alcoholic beverages. Even in therapeutics, the main value of alcohol is to be referred to its cerebral action.

It is often asserted that the conditions of life and the circumstances of many persons are such that the very moderate use of alcohol, in one form or another, is justified in consequence of its sedative action. Certainly there are many in whom the exacting duties, the friction and hurry of life have caused a state of mental tension and overwrought nerves, who find a good restorative in a glass of wine taken with their dinner at the close of the day's toil. The man who is so happily constituted that he can hold to a golden mean will not exceed his half pint of wine, even when he has no better reason for his indulgence than that he likes its taste and its mild mental effect.

From all the testimony that has been furnished both by science and empiricism, it would appear that the very moderate use of alcoholic beverages, the quantity not to exceed the equivalent of half a pint of table wine in the twenty-four hours, is physiologically permissible under the restrictions that have been laid down.

I am, however, far from holding the opinion that alcohol is an absolutely indispensable agent in medicine, or indispensable as a mental sedative, or as an adjunct to social life. As Partridge well says, the present use of alcoholics is not a necessity of social life ; they favor rather the overdevelopment of the social consciousness, and there is no reason derived from the evolutionary view why alcohol should not be entirely abolished from the world, and the craving which it satisfies be turned into some other channel. Its uses in the arts and industries alone, however, will long insure its presence in the world.

The studies of ethnologists have shown that the use of fermented drinks, hasheesh, mescal, and other stimulants which

powerfully affect the mind, had its origin in the fact that such agents greatly widen the range of emotional life. Primitive peoples seek this mental effect especially upon entering upon social or religious ceremonies, and this and other facts favor the conclusion of Partridge "that the impulse to seek intense states of consciousness is not an expression merely of a high state of nutrition, but a true instinctive tendency which has grown up as a necessary aid to mental development."

It is a question well worth considering, whether the continued presence of alcoholics in the world is not more conducive, in the long run, to the evolution of an efficient self-control, than would be their total abolition. Perhaps only an increasing knowledge of the properties of alcohol, joined with the exercise of that self control which is humanity's safeguard against all its vicious tendencies, can effect a fundamental cure of the drink evil.

BALTIMORE, November, 1900.

THE NUTRITIVE VALUE OF ALCOHOL.

BY

W. O. ATWATER.

THE NUTRITIVE VALUE OF ALCOHOL.

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CHAPTER VI.

(BY PROF. H. P. BOWDITCH.)

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CHAPTER I.

INTRODUCTION.

THE present report summarizes the results of an inquiry undertaken as part of the work of the Physiological Sub-Committee of the Committee of Fifty for the Investigation of the Drink Problem. The purpose of the inquiry was to gain information regarding the action of alcohol as food. The principal feature consists in a series of experiments made with men in the respiration calorimeter. The experimental work was done in the chemical laboratory of Wesleyan University. A large share of the expense was borne by the Committee of Fifty, although contributions were also received from the Elizabeth Thompson and Bache funds and from private individuals. The experiments were parallel with others of similar character, but without alcohol, which are conducted under the auspices of the United States Department of Agriculture. These latter experiments form a part of a general inquiry regarding the food and nutrition of man, which is authorized by Congress and prosecuted in different parts of the United States. The special inquiry into the nutritive action of alcohol was made possible by the generosity of Wesleyan University, which offered, for this purpose, the use of laboratory and other facilities that have been made available to the Department of Agriculture for the investigations on food and nutrition just mentioned.

The inquiry has been pursued with the active coöperation of a number of gentlemen including, especially, Dr. F. G. Benedict, who has been my chief associate in the experimental part of the inquiry; Mr. A. P. Bryant, under whose direction the results have been computed and tabulated; and Mr. A. W. Smith, Dr. O. F. Tower, and Dr. J. F. Snell, all of whom have been intimately associated with the elaboration of the methods and the carrying out of the details of the inquiry. Mr. Smith and Dr. Snell served as subjects in several of the experiments,

though the subject of the larger number was Mr. E. Osterberg. Important assistance has been rendered by Mr. O. S. Blakeslee in the devising and making of special apparatus; by Dr. W. J. Karslake, E. Osterberg, and H. M. Burr in the chemical work, by Mr. H. E. Bidwell in the recording and computing of the results, and by Dr. Paul Murrill in preparing the material for publication.

PLAN OF THIS REPORT.

A summary of the results of similar experimenting elsewhere has seemed desirable to aid in the interpretation of the experiments here reported. Such a treatise was prepared by the writer with the coöperation of Drs. H. C. Sherman and Alice H. Albro, but proved too voluminous for publication here, and in its place an abstract is given in the second chapter of the present report. It is hoped that the summary as a whole may be published elsewhere. The description of our own experiments and the main conclusions derived from them form the third and most important chapter. The details of the experiments, which are far too extensive for such a volume as the present, have been published in bulletins of the United States Department of Agriculture, and especially in a Memoir by the National Academy of Sciences, as stated in the explanations appended to Table I. on page 239. A summary of the plan and the results is given here.

In the lack of a brief compendium, in English, of the latest information concerning the nutritive value of alcohol, and the chemical composition and properties of the more common alcoholic beverages, the fourth and fifth chapters have been added. In the selection of the material for these, I have been influenced by inquiries which have come to me from many sources, and have sought to answer them as well as the limits of this volume and my own knowledge of the subject would permit. Some closely related and very important topics, such as the relation of alcoholic beverages to digestion, their action upon the brain and nervous system, and the pathological aspects of the subject generally, are not included, since they are treated in the other special reports which, together, make up the whole report of the Physiological Sub-Committee.

Many so-called "temperance drinks" contain so much alco-

hol, and are so freely used by the community (often under the impression that they are non-alcoholic) that it has been thought best to introduce a notice of this subject into the report on the nutritive value of alcohol. To this end an investigation of the question has been made under the direction of Dr. H. P. Bowditch, and the result is given in the sixth chapter of this report.

CHAPTER II.

RESULTS OF OTHER INQUIRY.

Topics to be considered.

THE results of experimental inquiry upon the nutritive action of alcohol may be considered under the following heads: the effect of alcohol upon digestibility of food; the proportion of alcohol oxidized and unoxidized; the effect upon the elimination of carbon dioxide and the consumption of oxygen; the metabolism of the energy of the alcohol; the protection of body fat and protein by alcohol; its effect upon the radiation of heat from the body and changes in body temperature; the rapidity of oxidation of alcohol in the body; and finally alcohol as a source of heat and of muscular energy. All these topics will be considered in chapter iii. which treats of our own experiments; but in considering the results of other experiments in this chapter the list of topics may be confined to:—

1. Elimination *vs.* oxidation of alcohol.
2. Effect of ingested alcohol upon the consumption of oxygen and elimination of carbon dioxide.
3. Protection of body material.
 - a. Protection of fat.
 - b. Protection of protein.
4. Utilization of alcohol by invalids and by habitual users.

The effect of alcohol upon digestion may be considered from two standpoints, one being the secretion of digestive juices and their action upon food, and the other the proportions of nutrients absorbed. The first of these subjects is discussed elsewhere by Professor Chittenden,¹ the second is treated in chapter iii. The remaining subjects have received so little attention from experimenters that the results may be conveniently treated under other heads.

¹ In vol. i. of the present report of the Physiological Sub-Committee of the Committee of Fifty.

Elimination vs. oxidation of alcohol.

The question here is this: Is alcohol burned, *i. e.*, oxidized, in the body like ordinary food? When bread, meat, and other common food materials are eaten, small portions escape oxidation. These residues are excreted by the intestine, but the larger part of the organic material of ordinary diet (95 per cent. or thereabouts) is burned in the body. When alcohol is taken its odor appears in the breath, and small quantities are also found in the urine. The question is, how does alcohol compare with ordinary food materials in respect to its oxidation and elimination?

Of the experimental inquiries on this subject which have come to our attention twenty seem of enough importance to call for special notice. Arranged in chronological order, they are: those of Frerichs (1), 1846; Bouchardat and Sandras (2), 1847; Klencke (3), 1848; Lallemand, Perrin, and Duroy (4), 1860; Baudot (5), 1863; Anstie (6), 1864; Sulzynski (7), 1865; Schulinus (8), 1868; Anstie (9), 1867; Thudichum (10), 1868; Subbotin (11), 1871; Dupré (12), 1872; Béchamp (13), 1872; Anstie (14), 1874; Heubach (15), 1875; A. Schmidt (16), 1875; Bodländer (17), 1883; Vogelius (18), 1885; Strassman (19), 1891; and Benedicenti (20), 1896.

These investigations were all European and nearly all French, German, or English. The experiments of Sulzynski and Schulinus were performed with blood outside the body; those of Subbotin and Schmidt were with rabbits; those of Lallemand, Perrin, and Duroy, of Anstie and of Bodländer with both men and dogs, and the rest were with men.

After the alcohol had been administered, tests for alcohol, and sometimes for products of its partial oxidation, as aldehyde and acetic acid, were made in the respired air, the urine, and, in a few cases, the feces, thus showing whether either the unchanged alcohol or the products of its incomplete oxidation were given off by the lungs and skin, kidneys, and intestine. In some instances the animals were killed, either by large doses of alcohol or otherwise, and tests were made for alcohol or its oxidation products in the different organs.

The observations previous to 1860 were made for the most part by methods which would now be considered crude, but are of interest because the results harmonize with conclusions which to-day stand unquestioned. Of the above twenty experiments, extending over a period of half a century, all but two were regarded by their authors as indicating that the ingested alcohol was more or less completely burned in the body. The two exceptions were those of Lallemand, Perrin, and Duroy, in 1860, and of Subbotin in 1871.

Lallemand, Perrin, and Duroy made several series of experiments with men and dogs. The doses of alcohol were generally large; with the dogs they were in some instances fatal. The tests for alcohol were made mostly by the use of potassium chromate, which reveals very minute quantities. In the excretions of the lungs, skin, and kidneys they found enough alcohol or other reducing material to be recognized by the chromate test and sometimes by distillation also. They also found similar traces of alcohol in the organs of dogs killed shortly after the alcohol was administered, but did not find evidence of the presence of aldehyde, acetic acid, or other residues from the partial oxidation of the alcohol. From the facts that they found some alcohol given off from the body unoxidized, and that no considerable quantities of products of partial oxidation were found, they inferred that the greater part of the alcohol was eliminated unchanged.

The experiments of Lallemand, Perrin, and Duroy were carried out in much detail, but it is evident that their conclusions were wrong. They ignored the fact that the quantities of alcohol in the excretions were minute as compared with the quantities taken, and made no attempt to measure the total amount given off unoxidized. They were evidently unaware of the fact, pointed out by later observers, that materials which give the chromate test are given off from the body when no alcohol has been taken. They simply jumped to the conclusion that the alcohol in their experiments was not oxidized, but was retained in the body until it was finally excreted. They claimed that it was given off completely and unchanged, or, to use their expression, "*en totalité et en nature*." The fallacy of their reasoning was speedily pointed out by other investigators. In 1863 Baudot showed that mere traces of alcohol suffice to give the chromate reaction, and that in none of the experiments of Lallemand, Perrin, and Duroy was the alcohol recovered from the excretions or from the organs more than a very minute proportion of that ingested; so that the authors' conclusions were by no means justified by their observations. He also recorded a number of experiments upon himself, showing the proportion of alcohol eliminated to be extremely small. Anstie also subjected the work of Lallemand, Perrin, and Duroy to critical examination, and showed that the experiments were crude and the conclusions erroneous.

Subbotin's experiments were made in 1871 with rabbits. The quantities of alcohol were large, being equivalent in some cases to about a pint of whiskey as a dose for an average man. When the animals could not be made to swallow the alcohol, it was administered by force through an incision in the œsophagus. The proportions given off unoxidized were not exactly determined, but it was estimated that

the amount so eliminated during the first twenty-four hours after ingestion was about sixteen per cent. of the total amount taken. From these data the author inferred that the most of the alcohol was sooner or later given off unconsumed. The fallacy of this conclusion was shown later by Anstie and Dupré, who pointed out that rabbits are not good subjects for such experimenting, since they do not endure alcohol well; that in view of the surgical operation performed and the enormous doses of alcohol given, these experiments are so abnormal and unreliable as to be of no real value; and that even if the experiments were satisfactory Subbotin's interpretation of the results is entirely unwarranted, since the elimination of alcohol practically ceases within the first twenty-four hours after ingestion. If we assume with Subbotin that sixteen per cent. of the alcohol was given off unoxidized within twenty-four hours, the inference in the light of our present knowledge would be that practically all of the remaining eighty-four per cent. was oxidized.

It is a frequent observation that when abnormally large quantities of ordinary food materials are taken into the body, the quantity which passes through the intestine undigested is considerably increased, and in cases where excessive amounts of sugar are taken it may even appear in the urine. It is therefore not strange that much alcohol should appear in the excretions after such excessive doses as Subbotin administered.

Between the years 1865 and 1874, Anstie, Thudichum, and Dupré made a large number of careful and exhaustive experiments with men and animals, the results of which leave no room for doubt that the amount of alcohol ordinarily eliminated by all the excretions is only a small fraction of that ingested, even when the quantities taken are rather large.

Since the final publication of Anstie's experiments and conclusions, in 1874, there has been no question among physiologists that ingested alcohol is for the most part oxidized in the body. The only question has been as to how completely the alcohol is burned. Several investigators have attempted the exact determination of the amounts which escape oxidation. Among these may be mentioned Heubach and A. Schmidt in 1875, Bodländer in 1883, Vogelius in 1885, Strassman in 1891, and Benedicenti in 1896. The amount of alcohol recovered from the excretions ranged from seven to one per cent. of the amount ingested. As the methods of determination have been refined, the apparent amount of alcohol eliminated has been smaller, probably because the excretions normally contain other substances which are likely to be confused with alcohol. The conclusion is, therefore, that as alcohol is ordinarily taken, nearly all is oxidized in the body.

The reason for treating of this subject at such length is that the theory that alcohol is not oxidized in the body has been frequently and constantly maintained, even since it was so thoroughly disproved.¹

Effects of ingested alcohol upon the consumption of oxygen and the oxidation of carbon.

This subject in its various phases has been much discussed. It has been vigorously maintained that alcohol reduces the consumption of oxygen and prevents oxidation of carbon and production of carbon dioxide in the body, and these views have been made the basis of an argument that alcohol cannot be useful for nutrition. But each of these forms of action has been no less strenuously denied. Experimental evidence is adduced on both sides. In like manner the power of alcohol to protect body fat from consumption has been both affirmed and denied.

The difficulty appears to be partly in a misapprehension of the subject and partly in the incompleteness of the experimental evidence. In discussing the general subject we have to consider: (1) the consumption of oxygen, (2) the production and the elimination of carbon dioxide, and (3) the gain or loss of carbon and the corresponding storage or loss of fat in the body.

Alcohol has been assumed to affect these processes in two ways. One is by its pharmacodynamic action referred to beyond. This is exercised, in part at least, through the nervous system, and is assumed to result in a retardation or inhibition of either the oxidation of carbon or the elimination of the carbon dioxide produced, or both. That alcohol in large enough quantities can retard the vital functions, and even cause death, is well known; the question here is as to its action, not in toxic doses, but in such amounts and forms as are used by ordinary drinkers. It is possible that in its action as drug, alcohol may sometimes have the opposite effect, that of increasing carbon metabolism, but I know of no positive evidence of such action.

The other way by which alcohol can affect the processes of metabolism is by being oxidized like other ingredients of food, as sugar, starch, and fat. This we may here call its direct action upon metabolism, or its nutritive action. It would seem natural that when it is oxidized in the body the production of carbon dioxide might be either diminished or increased, according as to whether (1) the alcohol takes the place of such materials as sugars, starches, and fats, which would otherwise be burned, or (2) is burned independently of other material, so that the total oxidation within the body is in excess of what would otherwise occur.

¹ See footnote on page 290.

If alcohol replaces the isodynamic amount of sugar, or starch, or fat, less carbon dioxide will be produced. Suppose, for instance, that enough alcohol be burned to furnish 100 calories of energy. The amount would be 14.15 grams, which would contain 7.38 grams of carbon. This carbon when oxidized would yield 27.04 grams of carbon dioxide. The isodynamic quantity of starch, *i. e.*, the amount which, if burned completely, would supply the 100 calories of heat or equivalent energy in other form in the body, would be 23.81 grams. This would supply 10.58 grams of carbon, which would yield 38.78 grams of carbon dioxide. If then the alcohol is oxidized, instead of the isodynamic amount of starch, the production of carbon dioxide would be reduced in the proportion of 39 to 27, or about one third. If the alcohol is burned instead of sugar the reduction will be nearly the same. If it replaces the isodynamic amount of fat (10.48 grams, containing 7.98 grams of carbon), the decrease in carbon dioxide will be small, since the isodynamic amount of fat would yield only 29.24 grams of carbon dioxide as compared with the 27 grams which would come from the alcohol. The starches and sugars make up the larger part of the nutritive material of food. If the alcohol is taken with ordinary food and in such way that less of the latter is oxidized, the production of carbon dioxide would naturally be lessened. This is equivalent to saying that if the alcohol oxidized contains less carbon than the material which it replaces, less carbon dioxide will result. If, on the other hand, the alcohol is burned without any reduction in the amount of other material burned, then more carbon dioxide will be produced with the alcohol than without it.

Late experimental inquiry indicates that either of these conditions may obtain when alcohol is ingested. Accordingly we should expect that the direct effect of the alcohol might be either to increase or to diminish the production of carbon dioxide. Either result might accompany the oxidation of the alcohol and neither would necessarily imply any tendency of the alcohol to retard oxidation of other materials except by being itself oxidized in their stead. That is to say if less carbon dioxide is produced with alcohol than without it, it does not necessarily follow that the alcohol exercised any inhibitory influence through its action upon the nervous system. These considerations have been neglected by earlier experimenters, as is natural, since they are the first of late inquiry.

Another important outcome of late experimental research is the evidence that the production and elimination of carbon dioxide are much more readily and largely influenced by even slight muscular movements than was formerly supposed. Indeed, we are coming to understand that the consumption of oxygen, the production and elimi-

nation of carbon dioxide, and the storage or loss of fat, are affected by a variety of factors, physical and physiological, the full influence of which has not been appreciated.

Still another factor, which has not been fully appreciated, is the influence of the nervous condition upon metabolism. Just when, how, or to what extent this is exerted is not yet clearly understood. It may be less important in the metabolism of carbon than of nitrogen. But it is a factor that should not be overlooked, because it may be more effective than has been supposed.

And finally, the earlier methods of inquiry were often defective in that the experimental periods were short, and the individual experiments were not repeated often enough to show how much of the observed effect was due to the alcohol and how much to other factors. In many cases the food was not analyzed, and in none of the experiments cited in this chapter do the data show the complete balance of income and outgo of nitrogen, carbon, and energy which is desirable, and indispensable for decisive results.

It is not strange that many of the older and some of the later experiments were planned and carried out in such ways as to make the results more or less inconclusive. Indeed, it is only within a few years that the apparatus and methods of determining the income and outgo of the body have been so developed as to make a reliable balance of energy possible, and even the determination of the total income and outgo of carbon requires facilities which are at the disposal of comparatively few investigators.

Experiments on the effects of alcohol upon the oxidation of carbon.

The experiments which I have found, and which seem to call for special consideration here, may be divided into four groups:—

1. Those upon the elimination of carbon dioxide only.
2. Those upon the consumption of oxygen only.
3. Those in which the elimination of carbon dioxide, the consumption of oxygen, and the respiratory quotient were observed.
4. Miscellaneous experiments.

They were made between the years 1813 and 1901. The whole number of the investigations here considered is 25, of which 12 belong to the first, 3 to the second, 8 to the third, and 2 to the last of the above groups.

1. *Experiments upon the elimination of carbon dioxide alone.*—The list includes investigations by Prout (21), 1813; Fyfe (22), 1814; Berzelius (23), 1838; Vierordt (24), 1845; Böcker (25), 1849; Duchek (26), 1853; Hammond (27), 1856; E. Smith (28), 1859; Setschanow (29), 1860; Berg (30), 1869; Vogelius (18), 1885; and

Bjerre (31), 1899. Of these experiments those of Vogelius were with rabbits, and the rest were with men.

Of the above experimenters the earlier ones, from Prout in 1813 to Hammond in 1856 inclusive, found in general less elimination of carbon dioxide in the exhaled air after alcohol had been taken than without alcohol. Hammond found that the taking of alcohol during a number of successive days was followed by an increase of body weight. He concluded "that alcohol increases the weight of the body by retarding the metamorphosis of old tissues, promoting the formation of new, and limiting the consumption of fat."

In 1859 Edward Smith made a considerable number of experiments with various alcoholic beverages. His results were rather different from those of the early observers. He states that alcohol always increased the evolution of carbonic acid gas to the extent of less than one grain (.0648 gm.) per minute. Rum also commonly had the same result, and good malt liquors produced an increase sometimes exceeding one grain per minute during more than two hours. Sherry wine commonly gave a small and constant increase. Brandy and gin, particularly the latter, lessened the quantity of carbonic acid evolved, while whiskeys varied in their effects. Inhalations of the volatile elements of alcohol, spirits, and wines caused a diminution in the quantity of carbonic acid gas and an increase in the vapor exhaled by the lungs.

In the experiments of Setschanow the production of carbon dioxide was diminished, and in those of Berg it was increased after taking alcohol. Vogelius experimenting with rabbits found that with doses corresponding to from 3.2 to 7.2 gms. per kilo body weight (the equivalent of 224-504 gms. for a man of 70 kilos) the elimination of carbon dioxide was diminished by 15 to 19 per cent. When the doses were increased so as to range from 6.6-12.2 gms. per kilo body weight (462-854 gms. for a man of 70 kilos), the elimination of carbon dioxide was increased by 16 to 69 per cent.

Bjerre, in experiments with himself in the Sondén-Tigerstedt respiration apparatus, exhaled in one day with ordinary diet 748.4 gms. of carbon dioxide. On the following day he took in addition to this diet 407 gms. of cognac (containing 167.6 gms. of absolute alcohol) in six unequal portions, and exhaled 779.6 gms. of carbon dioxide. He estimated that on the alcohol day the body spared 51.8 gms. of fat, and 71.8 gms. of carbohydrates; that is, it burned less by these amounts of materials with the alcohol than without it.

2. *Experiments upon the consumption of oxygen alone.* — Experiments on this subject were made by Harley (32) in 1864, Schmiedeberg (33) in 1868, both with blood outside the body, and Henrijean

(34) with men in 1883. Harley observed that the addition of 5 per cent. of pure alcohol to blood decreased the power of the latter to absorb oxygen, and give off carbon dioxide. Schmiedeberg, using slightly different methods, obtained confirmatory results. It is to be observed that in Harley's experiments the quantity of alcohol added to the blood was very large as compared with the quantities ordinarily taken in drinking.

Henrijean's experiments were made with a healthy young man in a respiration apparatus. Each experiment lasted only 15 minutes. As the average of a considerable number of experiments the oxygen absorption after taking alcohol was about the same as that after taking bread, and that in both cases it was about one fifth larger than when no food at all had been taken. In other words, when extra material was burned in the body, whether bread or alcohol, extra oxygen was used to burn it.

3. *Experiments in which both the consumption of oxygen and the elimination of carbon dioxide were determined.* — Experiments of this kind were reported by Boeck and Bauer (35) in 1874, Wolfers (36) in 1883, Futh (37) in 1885, Bodländer (38) in 1886, Desplats (39) in 1886, Zuntz (40) in 1887, Geppert (41) in 1887, and Chauveau (42) in 1901.

Of these experiments those of Desplats were with rats; those of Boeck and Bauer and of Chauveau were with dogs; Wolfers with rabbits; Futh and Bodländer with both dogs and rabbits; and those of Zuntz and Geppert were with men.

The investigations of all of these are of considerable interest. Speaking generally, they are superior in method to the experiments in which carbon dioxide only or oxygen only was determined, though here again the value is somewhat diminished by the shortness of the duration of the respiration experiments and by the omission of the other determinations necessary for a complete knowledge of the income and outgo of matter and energy.

In their indications of the effect of alcohol on the elimination of carbon dioxide, these experiments, like those previously cited, vary greatly one from another. Even experiments with the same species of animals and approximately the same quantities of alcohol sometimes give different results. Thus Boeck and Bauer found that 2.1 g. alcohol per kilo body weight increased the excretion of carbon dioxide and (estimated) consumption of oxygen by dogs, while Bodländer, also experimenting with dogs, found that 2.4 g. alcohol per kilo produced a decrease of 19 per cent. in both carbon dioxide excretion and oxygen consumption. As already pointed out, the quantities of alcohol used in the experiments with animals other than men were usually much

greater in proportion to body weight than the quantities ordinarily consumed by men. The results obtained by Zuntz and Geppert imply that alcohol in moderate quantities had no very marked effect upon the excretion of carbon dioxide by men. Zuntz found a slight increase, Geppert no change, or, if anything, a slight decrease.

Chauveau performed an extensive series of experiments with dogs in order to determine the effects of alcohol as compared with sugar in the animal's diet in work experiments. In the non-alcohol period the daily ration consisted of 500 grams of raw meat, and 252 grams of sugar. In the alcohol period 48 grams of alcohol was substituted for an isodynamic amount (84 grams) of sugar. The series of experiments lasted four weeks, and each ration was given for a week at a time, and in alternate weeks. The whole day's ration was given at one meal in the morning, and immediately afterwards the dog was set to work upon a treadmill driven by a water motor, where he ran for one or two hours. No analyses of food, feces, or urine are reported, and presumably none were made. On certain days the amounts of carbon dioxide exhaled and of oxygen consumed were determined, and these figures furnish the data from which the respiratory quotients may be calculated. The remaining determinations were distance traveled during working period, and weight of the animal at beginning and end of the experimental days, and at certain other times during the day.

The respiratory quotients are tabulated below, and will be discussed later. The other figures of the author show (1) that even with vigorous urging the dog could not be made to travel as far on the alcohol days as on the days when he received no alcohol, and (2) that the animal gained weight with the sugar ration, and lost weight with the alcohol ration. The experiments have been interpreted by their author and others as showing that alcohol can neither protect body material nor be a source of useful energy in the body.

That the dog did not work as well with the alcohol as without it is not surprising. The dose of alcohol was 48 grams of absolute alcohol for a dog of 18 or 19 kilos weight, equivalent to about $6\frac{1}{2}$ ounces for a man of 70 kilos. The effect of such enormous doses was strongly narcotic, so that it was only by urging with whip and stick that the dog was made to perform as much work as it actually did. In fact, the author states that the object of his research was to find out whether the subject could "have the blood saturated" with alcohol, and work as well as he could without it. The results on this point, therefore, do not permit of any inference being drawn in regard to the effect of moderate amounts.

As regards the effect of alcohol upon body weight, it is to be noted

that there are no analyses of food or excreta, so that there is nothing to show how much of the gain or loss is protein, or fat, or water. The changes in the amount of materials in the alimentary canal, together with the changes in the amount of water in the tissues and fluids of the body, may easily have been greater than the changes in the amounts of body fat and protein. As has been clearly pointed out by Zuntz,¹ the tendency of sugar is to increase the store of body water. On the other hand, alcohol often has a marked diuretic tendency which might diminish the amount of water in the body to a considerable extent, so that a gain in weight with the sugar diet, followed by a loss in weight when alcohol was substituted for the sugar, does not show that this gain or loss was fat or other nutrient stored in the body.

In this connection it is interesting to note that Chauveau had previously² made experiments with dogs in which fats and sugar were compared. The conditions were similar to those in the alcohol-sugar series above mentioned, and the results show that with a given amount of sugar (121 grams) in the diet the animal gained in weight, while with an isodynamic amount of fat (51 grams), substituted for the sugar, the body weight either diminished or remained constant. The differences are not as striking as in the alcohol experiments, which is natural, since fat is not known to have any diuretic action.

The determinations of carbon dioxide exhaled and oxygen used were made for three (unequal) periods, which together made up the experimental day; the first being the working period of 1 or 2 hours; the second a day period of 9-11 hours, and third the night period of 11-13 hours. The author omits from his discussion all the figures except those of the working periods, and finds that the average respiratory quotient for the working periods was .963 in the sugar experiments and .922 in the alcohol experiments. He assumes that the oxidation of the alcohol and sugar ought to take place at the same rate or in the same proportion as they were administered, and neglecting entirely the oxidation of the constituents of the meat, he calculates that .763 would be the theoretical respiratory quotient for the alcohol period. Since this quotient is not found in any period, and owing to the difference between this figure and .922 he reasons that no considerable part of the alcohol was oxidized. He says, "the enormous deficit which these figures show in each case in the combustion of the ingested alcohol is in accord with what is known about its elimination unchanged (*en nature*) by the exterior excretories, particularly in the process of respiration."

A point of especial interest in these experiments is seen in compar-

¹ Du Bois-Reymond's *Archiv. Physiol. Abtheil*, 1898, 267.

² *Compt. rend. de l'acad. des sc.* 125 (1897), 1070.

ing the quotients for the different periods. The average results are tabulated herewith:—

Periods.	Respiratory quotient.	
	Ordinary ration.	Alcohol ration.
Working periods 1 hour each989	.946
Working periods 2 hours each948	.912
Working periods, average of all963	.922
Day periods after work926	.863
Night periods880	.877
Whole day923	.886

The quotients for the working periods are slightly smaller with alcohol than without, but are all over .91, and imply that the principal material burned was carbohydrate, — either sugar or glycogen. As the working period was prolonged, the quotient fell, and is smaller for a two-hour than for a one-hour period. For the remaining periods they were still smaller and imply the oxidation of more or less material other than carbohydrate, *i. e.* protein, fat, and alcohol. The quotients for the whole day are considerably smaller with the alcohol ration, as would naturally result from the burning of the alcohol, and they correspond very closely with the calculated quotients for the two rations after making due allowance for fat gained or lost to the body. The most interesting point is that with both rations during a period of work which followed shortly after the ingestion of meat, sugar, and alcohol, the material burned appeared to be mainly carbohydrate. The minimum quotient is found in the day period of the alcohol experiments. This, together with the fact that the quotients for the night periods are nearly identical with the two rations, implies that most of the alcohol was burned during the 9–12 hours after the working period, which accords with the very natural supposition that most of the alcohol would be burned shortly after its ingestion. Another very interesting inference is that no large amount was burned during the period of one or two hours immediately following the ingestion of the alcohol, which in these cases was a working period. Whether the material which furnished the larger amount of fuel burned in these cases was sugar or glycogen, or both, the experiments do not show. The experiments of Chittenden (64) with dogs show that alcohol may be absorbed from the stomach and very speedily after its ingestion, but the theory that alcohol is burned very rapidly in the body is not supported by Chauveau's experiments, nor can they be taken as a conclusive test of the fuel value of alcohol.

In respect to oxygen consumption the results of the experiments are, almost without exception, parallel to the results on carbon dioxide excretion, those experimenters who found an increase or a decrease in

the one function finding likewise an increase or a decrease in the other.

The respiratory quotient ($\text{CO}_2 \div \text{O}_2$) served to some extent as an index of the nature of the materials oxidized in the body. The ratios of the volumes of carbon dioxide produced to the oxygen necessary for the combustion of the ordinary nutrients and alcohol are as follows:—

Respiratory Quotients.

Carbohydrates	1.00	Protein (available) . .	0.81
Fats	0.71	Alcohol	0.67

The combustion of alcohol in place of or in addition to any of the ordinary nutrients should, theoretically, lower the respiratory quotient, but to produce an appreciable effect upon the quotient, either the alcohol must replace carbohydrates or the quantity of alcohol substituted for protein or fats must be large. It is, therefore, not surprising to find that all the above investigators, with the exception of Wolfers, failed to detect any influence of alcohol upon the respiratory quotient. Wolfers, experimenting with animals (rabbits) whose normal diet is very rich in carbohydrates, found the respiratory quotient decreased by alcohol.

4. *Miscellaneous experiments.*—Under this head are included those of Simanowsky and Schoumoff (43) in 1884; and Thompson (44) in 1885. Thompson sought an answer to the question whether alcohol can serve as food by attempting to ascertain whether more of a given quantity of food is excreted unchanged when the body is well nourished than when it is in need of nutriment. Two experiments were made with each of three men. The indications were that the alcohol was burned less completely, *i. e.* there was more alcohol in the urine, with the liberal diet. The author regards these experiments as incomplete, but as furnishing strongly presumptive evidence of the food value of alcohol.

Simanowsky and Schoumoff observed that the oxidation of benzene injected into the blood of rabbits, dogs, or men was diminished by the administration of alcohol.

Conclusions.—In drawing conclusions from these experiments and applying them to the effects of alcohol as ordinarily taken by moderate drinkers, we meet several difficulties:—

1. In most of the experiments with animals the quantities of alcohol were very large, large enough indeed to be often intoxicating, occasionally toxic, and in some cases fatal.

2. The experimental periods were generally short, in a number of cases continuing only a few minutes. In some instances this defect

was partially compensated by repetitions of the experiments, as for instance in those by Wolfers and by Zuntz.

3. There is in no case a complete balance of carbon, hydrogen, nitrogen, and energy.

4. The experiments take for granted that no oxygen is stored in the body for future use. While this assumption may be correct it can by no means be regarded as proven. Until we know definitely whether or not such storage of oxygen does occur the results of experiments of this kind will be more or less in doubt.

5. Finally, there is more or less conflict in the results obtained, not only by different experimenters, but in some cases by the same experimenter in different experiments under apparently similar conditions.

Taking the experiments all together the following conclusions seem warranted : —

1. There is no valid evidence that alcohol, in moderate quantities, has any effect upon oxygen absorption different from that of ordinary nutrients.

2. There is no evidence that alcohol in moderate quantities has any effect upon the oxidation of carbon or upon the elimination of carbon dioxide, different from that of ordinary nutrients.

In so far as the experiments agree and appear to be conclusive, the results may be explained by the two assumptions : First, that alcohol in small quantities is oxidized, its energy is transformed, and the resulting carbon dioxide is eliminated, as is the case with ordinary food materials like sugar, starch, and fat ; second, that on the other hand alcohol in large quantities may retard or diminish metabolism in general, and, with the rest, the oxidation of carbon and elimination of carbon dioxide.

General considerations.

Before discussing the investigations in detail it will be well to refer to some considerations regarding the general subject and some of the sources of error in experiment and inference which have not always received the attention they deserved.

Alcohol as food vs. drug. — Experiments described beyond show that alcohol is oxidized in the body and that its potential energy thus becomes kinetic and is utilized in various ways. In these respects alcohol is more or less similar to the fuel ingredients of ordinary food, *i. e.* the carbohydrates and fats. This nutritive action of alcohol may for our present purpose be called its direct action. It is equally well established, indeed the fact has been much longer known, that alcohol has a very different action, exercised partly or wholly through the nervous system, of which the most familiar form is found in drunkenness. It is believed that in this pharmacodynamic action alcohol

exercises a very important influence upon metabolism. This may be called its indirect action, as contrasted with its direct action just referred to. From the standpoint of the pharmacologist this pharmacodynamic action would perhaps be called its direct action, but it is here termed indirect because we are discussing the subject from the standpoint of nutritive value. We have thus a very clear distinction between alcohol as food and alcohol as drug. The failure to observe this distinction has led to errors in the planning of experiments and serious confusion in the discussion of the results.

Large vs. small quantities. — Another distinction too often overlooked is the difference between the action of large and small doses. It may be taken in small amounts by people in health (the quantity varying with the individual) without sensibly affecting the nervous system or any of the vital processes. In larger quantities, varying with the individual and the conditions under which it is taken, it causes intoxication. If the doses are large enough it is powerfully toxic or even fatal. In some of the experiments described beyond, such toxic doses have been given, although the results have been presented as if they would follow when only small quantities were used.

Sources of error. Lack of measurements and analyses. — In most of the experiments beyond, the conclusions are based upon a comparison of the income and outgo of nitrogen or carbon or both. In some cases the oxygen and respiratory quotient were determined, but in nearly all of the older and in most of the later investigations the number of factors quantitatively measured was small, and some of the most essential were ignored, or at best were only roughly estimated. In not a few cases the methods of analysis were none too reliable.

Again, the experimental periods have often been short; sometimes only a few minutes or a few hours when a day would have been hardly sufficient, and sometimes only a day when several days would have been necessary for accurate results. These defects, formerly ignored because not understood, have been brought into clear relief as a result of later and more critical research.

Experimental results vs. inferences. — Another misfortune, which is also by no means confined to experimenting upon the physiological action of alcohol, is the failure to distinguish between attested fact and justifiable inference, in other words the basing of conclusions upon insufficient if not unreliable data. A notable illustration of this is found in the experiments of Lallemand, Perrin, and Duroy, on the oxidation of alcohol in the body. The theories which deny nutritive value to alcohol on the grounds that it lowers the body temperature, that it cannot form organized protoplasm, and that it is a proteid poison, are other instances of the same kind of error.

PROTECTION OF BODY MATERIAL BY ALCOHOL.

The power of alcohol to protect body fat and protein from consumption has been both affirmed and denied, although for some years past the protection of fat has been pretty generally conceded. During the last half dozen years the question of protein protection has been discussed with great vigor and by many writers. Later as well as earlier experiments on the subject have brought conflicting results, but during the last three or four years several experimenters, taking advantage of past experience, have adopted plans and methods of inquiry by which the uncertainties of previous work have been avoided, and the question has been subjected to reasonably decisive tests. Accordingly there remains to-day scarcely any room for doubt that alcohol can and often does protect protein from consumption. There still remains a question, however, as to whether it may not at times have the opposite effect, viz.: to increase protein katabolism, and thus act as a proteid poison.

Inasmuch as the experimental inquiries thus far made do not serve to distinguish between the protection of body material and the protection of food, and since further they throw little or no light upon the gains or losses of glycogen and other carbohydrates or of mineral matters and water in the body, the present discussion will be limited to the protection of body fat and protein by alcohol.

The protection of body fat.

For determining whether the body gains or loses fat under a given régime, two methods are employed. By one of these methods the income and outgo of nitrogen and carbon are compared, and since such experiments involve the determination of the respiratory products they are called respiration experiments. The other method consists in taking several animals nearly alike; killing some of them and subjecting the bodies to analysis to determine the quantities of fat; subjecting the others to the desired régime or different régimes, and then determining the fat in the bodies. Assuming that at the beginning all the animals had the same quantities of fat, the amounts present at the end show the effect of the régime. Of course in experiments of both kinds experimental errors must be allowed for.

The experiments in which the effects of alcohol have been studied by either of these methods are limited both in number and in scope. With the exception of our own experiments described in the next chapter, the respiration experiments are mainly those in which only the respiratory quotient was determined, and do not afford sufficient data to justify any definite conclusions as to the protection of fat by alcohol.

The experiments of Strassman (19) in 1891 belong to the second class. He took several pups of the same litter, and kept them for two to three months upon the same diet except that a daily allowance of alcohol was given to some of the pups in addition to the ordinary diet. In two series of experiments the results were the same, viz.: at the end of the experiment the dogs that had received the alcohol had stored more fat, both relatively and absolutely, than the dogs kept upon the basal ration. The general growth of the animals not being especially affected by the alcohol and the storage of fat being markedly increased, the author concludes that alcohol tends to produce a storage of fat, either by direct transformation into the latter or by protecting other material from consumption and thus inducing its transformation into body fat.

Effect of ingested alcohol upon the metabolism of protein.

In considering whether or not alcohol acts as a protector of protein, we have first to consider the methods of experimenting and the sources of error. The latter have already been referred to in a general way, and only those sources of error will be mentioned here which have a special bearing upon this topic. The distinction already brought out between the pharmacodynamic and nutritive actions of alcohol must here be kept constantly in mind, and cannot be too strongly emphasized.

The questions stated. — The ordinary fuel ingredients of food, as starch, sugar, and fat, are known to protect body proteids from oxidation, in that when they are oxidized in the body the latter has less occasion to draw upon the proteids of its food or its own organized material. Alcohol is oxidized in the body, and its energy is made available. This is indicated in the experiments above described, and is clearly proven in our own experiments described in the next chapter. It would seem, therefore, that it ought to have a direct action in protecting body proteids unless that influence is counterbalanced by the indirect action exerted through the nervous system. If it protects protein, the question would be whether its effect is the same, or greater, or less than the effect of isodynamic amounts of the carbohydrates or fats.

The questions, then, are: (1) Does alcohol by its oxidation tend directly to protect the protein of food or body material from consumption? (2) Does it by its indirect action tend to increase or decrease protein katabolism? (3) Under what circumstances does the first or the second of these actions actually obtain, and may they occur at the same time, and thus tend to counteract each other? (4) On the whole, can and does alcohol in moderate doses protect body protein, and, if so, how does it compare in this respect with isodynamic amounts of fats and carbohydrates?

Experimental methods. Nitrogen balance. — It is the almost universal custom to strike a balance between the income of nitrogen in the food and the outgo of nitrogen in the feces and urine for a given period, and take this as a measure of the gain or loss of nitrogen in the body. The quantity of nitrogen gained or lost is multiplied by a given factor (generally 6.25), and the product is taken as the gain or loss of body protein.¹ Numerous experimenters assume that the nitrogenous material thus measured is true proteid. Others recognizing the facts that not all of the nitrogen of either food or body material is in the form of proteid, and that multiplying the amount of nitrogen by any factor may fail to give the exact amount of either total nitrogenous material or total proteid, prefer the term protein to designate the nitrogenous material as thus estimated. So far as the gain or loss of nitrogenous material in the body in ordinary experiments is concerned, the quantity of protein would probably differ very little from that of true proteids.

Gross vs. net gain or loss of nitrogen. — If the determinations of nitrogen in food, feces, and urine are correct, the difference between income and outgo of nitrogen must give a very nearly accurate measure of the total gain or loss of nitrogen to the body, since there is no other source of income than food (and drink), and no outgo outside of feces and urine except by perspiration and in the very small losses of skin and hair. The losses of nitrogen in perspiration may be appreciable with severe muscular exercise, but ordinarily they are too small to be taken into account.

The gains or losses of nitrogen, as thus determined, may be called the gross gains or losses. They do not represent the actual gains or losses of body material because they omit two variable and disturbing factors. One of these is the change in the amount of nitrogen in the alimentary canal during the period of the experiment. If we could begin and end the experiment with the alimentary canal empty, there would be no trouble from this source, but however careful we may be to have diet, exercise, and other conditions uniform, the quantity of nitrogen supplied by the food and still remaining unabsorbed may not be the same at the end as at the beginning of the experimental period. This means that the nitrogen of food and drink may not be the same as the amount which is absorbed through the walls of the canal, and

¹ The terms protein, proteids, and albuminoids are used somewhat indiscriminately to designate the more important nitrogenous compounds of the body. A common usage classes such substances as albumin of egg, casein of milk, myosin of muscle (lean meat), and the "gluten" of wheat as proteids, and groups these with other nitrogenous compounds under the generic name of protein.

which constitutes the real income of nitrogen to the body. The error thus introduced may be larger or smaller. It can be reduced to a minimum by two means : one is to have the beginning and the end of the experimental period at the same time of the day, preferably after a night's rest, and at the end of the longest period between meals, and the other is by making the experimental period as long as practicable.

A still worse difficulty is found in the lapse of time between the breaking down of proteid in the body and the excretion of the katabolized products in the urine. To this period the term "nitrogen lag" is applied. The time of this lag varies greatly, and we do not yet know by what conditions it is decided, or how long it continues in any given case. It is customary to take the nitrogen in the urine for a given period as a measure of the protein katabolized in that period. The error produced by the nitrogen lag may therefore be considerable. If the experiment be one in which the effect of alcohol is compared with that of ordinary food, the error may be increased by the diuretic action of the alcohol, which seems at times to materially accelerate the excretion of urea and other nitrogenous compounds.

The difference, therefore, between the nitrogenous material actually absorbed and that actually katabolized during a given period may be called the actual or net gain or loss of protein for that period, but this cannot be exactly determined because of the two disturbing conditions just named, viz. : (1) Difference in the amounts of unabsorbed nitrogen in the alimentary canal, and (2) difference in the amounts of katabolized nitrogen in the body due to nitrogen lag.

Temporary vs. permanent effect of alcohol. Acquired tolerance.—Considered as a drug the action of alcohol differs not only with the quantity ingested, but also with the power of the individual to resist its pharmacodynamic action. This resisting power often increases with use, so that a dose which would make a beginner drunk is tolerated by an habitual drinker without symptoms of intoxication. This acquired tolerance is very common, not only in the use of drugs, but in many other ways. It is very easy to see, therefore, that the effect of alcohol upon metabolism might change with its use. This seems to have actually been the case in some of the experiments upon the effect of alcohol upon the breaking down of protein in the body, notably those of Neumann, Clopatt, and Rosemann. The experiments which have been most commonly cited as evidence that alcohol does not protect protein are those of Miura, of Schmidt, and of Schoeneseiffen, referred to beyond. In these the alcohol periods were from four to six days each. In later experiments by Neumann, by Clopatt, and by Rosemann (second experiment), in which the experimental periods with alcohol have been made much longer, the alcohol has failed to

protect protein during the first four to six days, but thereafter the protecting power of alcohol has been clear and very marked. In still other experiments also made by late and reliable methods, including those by Rosenfield and Chotzen, by Ström, and by Rosemann (first experiment), the protein protection has been manifest from the outset, and has continued to the end. As will be explained in the more detailed reference to these experiments beyond, the results point to a difference between a temporary action of the alcohol in which it may fail to protect protein and a more permanent effect of protein protection. This temporary failure of the alcohol to protect protein is conveniently explained by the hypothesis referred to above, viz.: that in its pharmacodynamic action it may tend to increase protein katabolism. As will be seen later, the theory of the twofold action helps to reconcile the conflicting results of the earlier experimenting.

Unreliability of urinary nitrogen as a measure of the effects of different agencies upon protein metabolism. — The influence which the various uncertain or unknown factors exert upon the excretion of nitrogen in the urine is certainly much greater than has been commonly appreciated. I have been much surprised to find in the results of our own and other investigations the evidence of wide variations in the excretion of nitrogen and in the nitrogen balance where the real causes are obscure. My own confidence in the results of the experiments of a few days' duration as indications of the influence of any such agencies upon nitrogen metabolism was much shaken by the experience of Dr. C. F. Langworthy and myself in collating and comparing the results of experiments on these subjects in the course of the preparation by ourselves of Bulletin 45 of the Office of Experiment Stations of the United States Department of Agriculture, A Digest of Metabolism Experiments in which the Balance of Income and Outgo was observed. The tables of this volume include summaries of 2299 experiments with men and 1362 with animals, in which the nitrogen balance was studied. The very clear impression left upon my own mind is that a not inconsiderable share of the conclusions reached by the authors of this very large amount of painstaking inquiry must be held subject to revision in the light of inquiries in which the experimental periods will be longer, and the determinations more detailed.

Experiments on the effects of alcohol upon protein metabolism.

The summary¹ previously referred to includes references to thirty-six separate investigations made between the years 1849 and 1901, by Bocker (25), 1849; Hammond (27), 1856; Setschanow (29), 1860; E. Smith (45), 1861; Perrin (46), 1864; Obernier (47), 1869; Ra-

¹ See page 175.

bureau (48), 1870; Parkes and Wollowicz (49), 1870; Fokker (50), 1871; Parkes and Wollowicz (51), 1871; Parkes (52), 1872; Zülzer (53), 1876; Strübing (54), 1877; Munk (55), 1878; Riess (56), 1880; Vogelius (18), 1885; Weiske and Flechsig (57), 1886; Romeyn (58), 1887; von Jaksch (59), 1888; Weiske and Flechsig (60), 1889; Keller (61), 1889; Mogilianski (62), 1889; von Noorden and Stammreich (63), 1891; Chittenden (64), 1891; Miura (65), 1892; Ström (66), 1894; Schendrikowsky and Dombrowsky (67), 1894; Donogány and Tibáld (68), 1894; Fortmüller (69), 1897; Schmidt (70), 1898; Schoeneseiffen (71), 1899; Neumann (72), 1899; Rosenfeld and Chotzen (73), 1900; Clopatt (75), 1901; Neumann (76), 1901; Rosemann (77), 1901.

Of the above experiments, those of Weiske and Flechsig were made with sheep, those of Fokker, Zülzer, Strübing, Munk, Vogelius, Chittenden, and Donogány and Tibáld, with dogs; and the rest with men. They may for convenience be divided into three classes:—

(1) Those in which alcohol was given to fasting subjects or was added to an insufficient diet.

(2) Those in which alcohol was added to a diet sufficient for nitrogen equilibrium.

(3) Those in which a part of the carbohydrates or fats of a diet usually sufficient for nitrogen equilibrium was replaced by alcohol, the quantity of alcohol being sometimes, though not always, isodynamic with the materials which it replaced.

Not all of the experiments can be placed exactly in either of these categories, but the classification may, nevertheless, be used in a rough way for a general summary.

Experiments in which the subjects were fasting or had an insufficient diet except as they received alcohol.—The experiments in this category give no very definite results. Those of Fortmüller, with rabbits, showed an increase, and those of Romeyn with men, showed a slight decrease in nitrogen metabolism when alcohol was taken without other food. The addition of alcohol in abundant quantity to an inadequate diet in Schoeneseiffen's experiments with himself failed to check the loss of nitrogen from the body during six days.

Experiments in which alcohol was added to diets generally sufficient for nitrogen equilibrium.—In comparatively few experiments in this category has the addition of alcohol been followed by an increase in the excretion of nitrogen. Such an increase, however, was observed in the experiments of Perrin upon himself with fermented liquors, in those of Munk upon dogs with 2 to 2½ cc. of alcohol per kilo body weight, in those of Ström upon men with large quantities of alcohol, and in those of Weiske and Flechsig upon sheep. The opposite result,

namely, a smaller output of nitrogen with alcohol, was observed by Hammond, E. Smith, Obernier, Rabuteau, Reiss, von Jaksch, Mogilianski, Schendrikowsky and Dombrowsky, and Neumann, with men; and by Strübing, Munk (with small doses, $1\frac{1}{4}$ cc. per kilo body weight) and Vogelius, with dogs.

Parkes and Wollowicz, Parkes, Ström (with small quantities of alcohol), and Schmidt, with men; and Weiske and Flechsig in their first experiments with sheep, found that the addition of alcohol to an adequate ration was without apparent effect upon the excretion of nitrogen.

Experiments in which alcohol was substituted for fats or carbohydrates. — Of especial interest are the experiments in which alcohol was substituted for more or less nearly isodynamic amounts of either fats or carbohydrates or both. To this class belong those of Stammreich (von Noorden), Miura, Neumann, Chotzen (Rosenfeld), Clopatt, and Rosemann. These investigations agree in their outcome as to the effect of such substitution of alcohol for ordinary nutrients; in Chotzen's experiments protein protection was manifested from the outset; in nearly all the other cases there was an increased excretion of nitrogen for three or four days, and in Clopatt's experiment this increased output lasted six days. But in all the experiments in which the alcohol period was continued longer than six days, viz.: those of Neumann, Clopatt, and Rosemann, it was found that this increase in proteid metabolism was only temporary. In the experiments of Mogilianski the output of nitrogen was not materially altered by the substitution of alcohol for nearly isodynamic amounts of ordinary nutrients.

It is not easy to ascribe to each of the above investigations its exact relative importance. There are, however, a number which seem to me worthy of particular consideration, partly because of their intrinsic importance and partly because of the stress that has been laid upon them in current discussions of the subject.

Very fortunately two careful discussions of the whole subject have been lately published, one by Dr. Rosemann (77), of the University of Greifswald in Germany, which fills nearly two hundred pages, and one by Dr. Rosenfeld (74), which occupies a prominent place in a most excellent treatise upon the influence of alcohol upon the organism. Rosemann's article is especially interesting because its author is one of the ablest and most critical students of the subject, and previous to the publication of this article had been perhaps the leading exponent of the view that alcohol does not protect protein from consumption. In this treatise, however, he goes over the ground very thoroughly, and finds not only in some of the later experiments by others, but also in experiments of his own here published, very convincing evi-

dence that alcohol can and does under proper conditions protect protein in the body from katabolism. At the same time he adopts the theory suggested by Miura, that alcohol may induce proteid katabolism, and also the theory proposed by Neumann, that this action may be only temporary.

Rosenfeld's treatise is keenly discriminative, scholarly, and impartial. His conclusions, on the whole, are strongly opposed to the use of alcohol as a beverage, and would tend to materially restrict its use as a medicine, but he is as emphatic as Rosemann in the conclusion that alcohol may, and at times does, act as a protector of protein. As regards the disintegrating action of alcohol upon proteid, Rosenfeld is less certain. He finds that the addition of alcohol to the diet is frequently accompanied during the first days by an increased output of uric acid, although the total nitrogen in the urine may be diminished. Since uric acid is believed to be a cleavage product of nuclein, he infers that alcohol may induce katabolism of the nucleoproteids, while at the same time protecting the other proteids (albumins, globulins, etc.) from consumption; but owing to the lack of data regarding the income and outgo of phosphorus, which is characteristic of the nucleins, he does not consider this hypothesis proven. He attaches especial importance to the diuretic effect of the alcohol, and suggests that a washing out of the products of proteid cleavage may account for much of the increase of urinary nitrogen, which has been commonly taken to represent increased protein katabolism. He reaches the following definite conclusions regarding the influence of alcohol upon the metabolism of matter (*stoffwechsel*) in the body:—

“(1) It is certain that ninety per cent. of the ingested alcohol is burned in the body. (2) It is certain that after the ingestion of alcohol the amounts of carbon dioxide exhaled and oxygen used increase either imperceptibly or not at all. (3) It accordingly follows that alcohol acts as a protector of body material or food. (4) It is certain that alcohol always protects fat. It is certain that alcohol can protect protein.”

A discussion would be unsatisfactory without more especial reference to some of the experiments above referred to. As we have already seen, the earlier experiments brought conflicting results; some implying the protection of protein by alcohol, and others the opposite. Of the former class those of Mogilianski and of Parkes and associates are of especial interest.

Of the experiments which have been interpreted as opposed to the protecting power of alcohol, those of Miura, made under the direction of von Noorden, and those of Schmidt and of Schoeneseiffen, under the direction of Rosemann, have been much quoted. The general

plan of experimenting followed by these three investigators consisted in giving the subject an ordinary diet for a time and observing the nitrogen balance. Thereafter, during a period of four to six days, alcohol was used. In Miura's case the alcohol was substituted for carbohydrates in the diet, but with the alcohol the excretion of nitrogen increased and the body lost nitrogen. With Schmidt, alcohol was added to a diet with which nitrogen equilibrium had been maintained; the alcohol did not diminish the excretion of the nitrogen and the equilibrium continued. With Schoeneseiffen, alcohol was added to an inadequate diet with which there was loss of nitrogen; the loss continued with the alcohol. These results will be more clearly seen from an examination of the accompanying figures:—

Statistical Summary of Experiments of Miura, Schmidt, and Schoeneseiffen.

[Quantities per day.]

Period and ration.	Length of period.	Income.		Nitrogen excreted.	Nitrogen balance.
		Protein.	Energy.		
<i>Miura, first series.</i>	Days.	Grams.	Calories.	Grams.	Grams.
Fore-period, basal ration + carbohydrates	5	45.7	1820	9.25	—1.94
Alcohol period, basal ration + alcohol . .	4	45.2	1823	9.76	—2.47
After-period, basal ration + carbohydrates	4	45.2	1820	8.18	— .98
Control period, basal ration only	3	45.5	1361	9.37	—2.09
<i>Miura, second series.</i>					
Fore-period, basal ration + carbohydrates	6	98.6	1955	14.90	+ .89
Alcohol period, basal ration + alcohol . .	4	98.6	1955	17.46	—1.67
After-period, basal ration + carbohydrates	4	98.6	1955	15.30	+ .49
Control period, basal ration only	3	98.6	1493	16.99	—1.20
<i>Schmidt.</i>					
Fore-period, basal ration only	6	97.2	2517	15.31	+ .23
Alcohol period, basal ration + alcohol . .	4	97.2	3147	15.74	— .20
After period, basal ration only	4	97.2	2517	15.37	+ .18
<i>Schoeneseiffen.</i>					
Fore-period, basal ration only	5	83.4	2178	15.10	—1.76
Alcohol period, basal ration + alcohol . .	6	86.3	3099	15.44	—1.63
After period, basal ration only	3	83.3	2154	13.91	— .58

These experiments have furnished the chief basis for the contention that alcohol cannot protect protein. In Miura's case the increase of nitrogen excretion with the alcohol was slightly larger than when the carbohydrates were removed, and no alcohol was used in their place. Miura and after him Rosemann and others inferred that alcohol was unable to protect protein from disintegration, and they went so far as

to ascribe to it a positive disintegrating action and to apply to it the term proteid poison.

Neumann, in 1899, made experiments on a similar plan save that the alcohol period was continued for sixteen days, during which part of the fat of the normal diet was replaced by alcohol. He found that during the first four days of the alcohol period there was no evidence of protein protection, the nitrogen excretion was increased, and was as large as during another period when the ordinary ration was reduced, and no alcohol was used in its place. Thereafter the nitrogen excretion diminished, and during the remaining twelve days of the alcohol period it was the same as with the normal ration. When the alcohol was removed, and nothing substituted, the excretion of nitrogen increased as before. Neumann concludes that in his own case the failure of the alcohol to protect protein at first was probably due to a specific though temporary action by which it tended to increase the disintegration of protein, so that the tendency to protein protection was counteracted. Later this special action disappeared, and the protecting action came into full play. The results of Neumann's experiments are epitomized herewith.

Statistical Summary of Neumann's Experiments. First Series.

[Quantities per day.]

Period and ration.	Length of period.	Income.		Nitrogen excreted.	Nitrogen balance.
		Protein.	Energy.		
	Days.	Grams.	Calories.	Grams.	Grams.
I. Basal ration + fat	5	76.2	2682	11.93	+ .26
II. Basal ration only	4	76.0	1959	13.79	- 1.36
III. Basal ration + alcohol (first 4 days) .	4	76.0	2677	15.21	- 3.05
IIIa. Basal ration + alcohol (following 6 days)	6	76.0	2677	12.48	- .32
IV. Basal ration + fat + alcohol	6	76.2	3402	10.84	+ 1.35
V. Same as period II.	4	76.0	1959	14.06	- 1.90
VI. Same as period I.	6	76.2	2682	12.43	- .24

Neumann's interpretation of his experiments was questioned by Rosemann, who maintained the disintegrating, but questioned the protecting action of the alcohol, alleging defects in the plans of Neumann's experiments. Neumann, without replying, repeated his experiments in such ways as to meet Rosemann's objections, and found conclusive evidence of the protecting power of the alcohol; these later results being published early in 1901.

Statistical Summary of Neumann's Experiments. Second Series.

[Quantities per day.]

Period and ration.	Length of period.	Income.		Nitrogen excreted.	Nitrogen balance.
		Protein.	Energy.		
	Days.	Grams.	Calories.	Grams.	Grams.
I. Basal ration only	5	112.7	2590	17.98	+ .06
II. Basal ration + alcohol (first 6 days)	6	112.7	1	18.04	
IIa. Basal ration + alcohol (7th to 11th days)	5	112.7	1	16.82	+ 1.22
IIb. Basal ration + alcohol (12th to 18th days)	7	112.7	3310	16.06	+ 1.98
III. Basal ration + alcohol — fats	7	112.7	2583	18.25	— .21
IV. Basal ration + fats	6	112.7	3304	15.05	+ 2.42

In 1900, Chotzen, working under the direction of Rosenfeld, and in 1901, Clopatt, each published some experiments. Clopatt's results agreed with Neumann's views, while Chotzen's experiment indicated the protection of protein from the beginning of the alcohol period.

Statistical Summary of Experiments of Chotzen and Clopatt.

[Quantities per day.]

Period and ration.	Length of period.	Income.		Nitrogen excreted.	Nitrogen balance.
		Protein.	Energy.		
	Days.	Grams.	Calories.	Grams.	Grams.
<i>Chotzen.</i>					
I. Basal ration only	3	73.3	2732	12.41	— .68
II. Basal ration + 60 grams alcohol	2	73.3	3156	11.32	+ .41
IIa. Basal ration + 120 grams alcohol	2	73.3	3580	10.32	+ 1.43
III. Basal ration + 155 grams sugar	2	73.3	3346	10.62	+ 1.11
<i>Clopatt.</i>					
I. Basal ration + fats	12	100.9	2677	15.18	+ .96
II. Basal ration + alcohol (1st to 6th days)	6	102.1	2646	17.82	— 1.46
IIa. Basal ration + alcohol (7th to 12th days)	6	102.1	2638	14.81	+ 1.53
III. Basal ration only	7	99.8	2009	15.49	+ .48
IV. Basal ration + fats	5	101.1	2613	15.68	+ .50

Meantime Rosemann made several series of experiments of his own,

¹ During the first 12 days of the alcohol period the alcohol was taken in amounts gradually increasing from 20 to 100 grams per day, so that the energy of the daily ration ranges from 2734 calories on the first alcohol day to 3238 on the eleventh.

the outcome of which, to his surprise, clearly demonstrated the protecting power of alcohol, and confirmed the views maintained by Neumann.

Statistical Summary of Rosemann's Experiments.

[Quantities per day.]

Period and ration.	Length of period.	Income.		Nitrogen excreted.	Nitrogen balance.
		Protein.	Energy.		
<i>First series.</i>	Days.	Grams.	Calories.	Grams.	Grams.
I. Basal ration + fats + sugar	9	102.5	3316	15.62	+ 1.13
II. Basal ration + alcohol (1st to 4th days)	4	102.5	3441	16.58	+ .32
IIa. Basal ration + alcohol (5th to 14th days)	10	102.5	3441	15.71	+ .98
III. Same as in period I.	6	102.5	3316	15.84	+ 1.05
IV. Basal ration only	7	97.5	2416	16.85	- 1.46
<i>Second series.</i>					
I. Basal ration + fats + sugar	9	84.4	2914	14.26	-.89
II. Basal ration + alcohol (1st to 4th days)	4	76.9	3104	14.39	- 2.09
IIa. Basal ration + alcohol (5th to 10th days)	6	76.9	3104	13.31	-.84
III. Basal ration + sugar	5	71.9	2981	12.05	-.37
IV. Basal ration only	4	71.9	2079	14.05	- 2.37

In the above-mentioned summary of results of inquiry in this field, Rosemann assents fully to the interpretation placed by Neumann, Rosenfeld, Chotzen, and Clopatt upon their experiments, believes that the protection of protein is shown by other experiments, as those of Mogilianski, considers it fully demonstrated by his own experiments, and comes to the definite conclusion that alcohol has a twofold influence upon the metabolism of protein, as previously suggested by Neumann. He is inclined to believe with Neumann that the disintegrating action is most apt to occur with persons little accustomed to the use of alcohol, and is of short duration, while in its action as a protector of protein it is analogous to the carbohydrates and fats, its influence being due to the utilization of its energy by the body. According to this view the results obtained by Miura and others, in whose experiments the alcohol periods continued only from four to six days, are explained by the disintegrating action of the alcohol which counteracted the protecting action, so that the resultant effect was an apparent failure of the alcohol to protect protein. With Neumann the alcohol periods continued after this disintegrating action ceased, and showed the more permanent protecting influence. The fact that in a number of the experiments the protecting influence was manifested

from the start is explained by the absence or only partial action of the disintegrating tendency.

We have then a clearly defined theory regarding the influence of alcohol upon proteid metabolism. This theory assumes two different kinds of action of alcohol. In the one it is a direct protector of protein and serves the body as food; in the other it tends to disintegrate protein and acts as a drug. The belief in the first action follows as a corollary from the oxidation of alcohol in the body and the transformation of its energy. In undergoing these changes alcohol is similar to sugar, starch, and fat, which, by their own oxidation and consequent supply of energy to the body are able to protect the constituents of the food and of the body, including protein, from oxidation. That alcohol may and does protect protein is abundantly demonstrated by the experiments above cited.

Other phases of the question.—In late discussion the relation of alcohol to the metabolism of proteids and to protoplasm has been made the basis of two special arguments regarding its value in nutrition. The two are sometimes put together, but are clearer when separated. One is that alcohol is not a protector of protein, but is a proteid poison and hence cannot be serviceable as food.¹ With the proof that alcohol can and does protect protein this reasoning fails.

The other is in substance this: In order that any substance may serve a useful purpose as nutriment it must first become a part of organized protoplasm. Alcohol cannot be so organized. Therefore alcohol cannot serve as nutriment.² The theory that proteid material must be organized in order to be efficient has some experimental basis, though it is in dispute among physiologists. That the fats and carbohydrates must be so organized in order to be effectively utilized is even more doubtful. Whether alcohol can or cannot be thus organized is a question still undecided by experiment. Considering the argument as a syllogism, the major premise is unproven and doubtful, the minor premise hypothetical, and the conclusion directly opposed by experimental fact.

Is alcohol a proteid poison?—The disintegrating influence of alcohol upon protein is less definitely proven, and hardly more than a convenient hypothesis for explaining the failure of alcohol, under some circumstances, to protect protein.

On the supposition that alcohol does at times induce the katabolism of protein, it has been called a "*proteid poison*." The question arises,

¹ See Kassowitz, *Allgemeine Biologie*, vol. i. pp. 49–60. See, also, Forel, vol. i. p. 83, of this report.

² See Kassowitz, *loc. cit.* p. 197, and *Deutsch. med. Wchnschr.* 1900, Nos. 32–35.

What is the experimental evidence of this disintegrating influence of alcohol upon protein compounds in the body?

If experiments can be adduced to show that, with rations and under conditions otherwise the same, the addition of alcohol is followed by increased proteid katabolism, in other words, that more protein is broken down with alcohol than without it; and if the excess is clearly beyond the limits of experimental error; and if the number of such results is sufficient, the principle may be regarded as established. The available evidence is in the experiments above cited, but in its consideration only those should be included in which the analyses of both food and excreta, that is to say the income and outgo of nitrogen in the body, were actually determined.

The accompanying table comprises all of the experiments that we have found which fulfill the last condition, and includes the only two series of our own experiments in which a ration containing alcohol was compared with a ration otherwise the same except that the alcohol was left out. It will be observed that the figures for the first day of each experiment are omitted in calculating the averages as given in columns five and six of the table, and the differences which are taken as indications of the effects of the alcohol are calculated from these averages. The reason for this is that in a number of cases the nitrogen output for the first day was very clearly influenced either by the previous diet, or the change in diet or other disturbing factor, and it is here assumed, whether justly or not, that the results will be more fairly comparable if the figures for nitrogen outgo for the first day after a change of ration are omitted in all cases. The omitting or including of the figures for a single day sometimes makes a decided difference in the result. In some cases, also, there is a question as to how the periods shall be compared. Thus in the experiments of Schoeneseiffen there are three periods with the same basal ration, viz., a fore-period of five days and an after-period of three days with basal ration only, and an intermediate period of six days with alcohol added to the basal ration. If the alcohol period is compared with the fore-period an apparent protection of protein is shown; if it is compared with the after-period (as is done by Rosemann), an increased katabolism due to alcohol is indicated; but if the first day is omitted from each period and the remaining days averaged together, and then compared with the alcohol period (as is done in the table), the result shows neither protection nor the opposite. This is one of the numerous cases which illustrate the uncertainty of the comparisons in this kind of experimenting.

Statistical summary of experiments where alcohol was added to ordinary ration.

[Quantities per day.]

	Alcohol period.	Average daily gain or loss of nitrogen.				Nitrogen spared by alcohol.
		First day included.		First day omitted.		
	Total duration.	Part here considered.	Basal ration plus alcohol.	Basal ration only.	Basal ration plus alcohol.	Basal ration only.
CLASS I. SHORT PERIODS AND FIRST DAYS OF LONG PERIODS.						
<i>Group A. Apparent increase in protein katabolism:</i>						
Neumann, Series I., periods 2 and 3.	12	Days.	Grams.	Grams.	Grams.	Grams.
Mura, Series I.	16	first 6 days.	-1.46	+ .48	-1.82	+ .17
	4	first 4 days.	-3.05	+ .63	-2.79	-1.86
		all.	-2.47	-2.69	-2.78	-2.26
<i>Group B. Elimination of nitrogen not affected by addition of alcohol:</i>						
Rosemann, Series II.	10	first 4 days.	-2.09	-2.37	-2.40	-2.72
Ström, Series II.	3	all.	.79	-1.49	.85	.10
Schoeneseiffen.	6	all.	-1.63	-1.32	-1.60	-1.62
Mura, Series II.	4	all.	-1.67	-1.20	-2.19	.02
Neumann, Series II.	25	first 6 days	- .92	+ .06	+ .08	+ .11
Schmidt	4	all.	- .20	+ .21	- .14	- .05
<i>Group C. Protein protection manifested from the outset:</i>						
Rosenfeld-Chotzen.	4	all.	+ .92	- .68	+ 1.13	- .68
Ström, Series I.	4	all.	.36	-2.18	.45	-1.44
Rosemann, Series I.	14	first 4 days.	+ .32	-1.46	.47	-1.53
Atwater and Benedict, Exp. 22, 23.	4	3	+ 1.38	- .30	+ .23	- .35
CLASS II. LAST PART OF PROLONGED ALCOHOL PERIOD.						
<i>Protein protection in every case:</i>						
Rosemann, Series I.	14	5th to 14th.	+ .98	-1.46	+ .98	-1.53
Rosemann, Series II.	10	5th to 10th.	.84	-2.37	.84	-2.72
Cloppatt.	12	7th to 12th.	+ 1.53	+ .48	+ 1.53	+ .17
Neumann, Series I., periods 2 and 3.	16	5th to 10th.	.32	-1.63	.32	-1.86
Neumann, Series I., periods 4 and 6.	16	11th to 16th.	+ 1.35	- .24	+ 1.49	- .12
Neumann, Series II.	25	7th to 18th.	+ 1.43	+ .06	+ 1.75	+ .11
Atwater and Benedict, Exp. 18-21.	10	2	- .50	- .90	- .06	-1.35

¹ Alcohol was administered on the last day preceding Exp. 22.

² An alcohol period of four days preceded Exp. 18.

The figures in the last column, "nitrogen spared by alcohol," are obtained by subtracting the figures of the sixth from those of the fifth column. The plus sign indicates an apparent protection, and a minus sign apparent disintegration. Class I. refers to the first 4-6 days of the alcohol period, as compared with a control period of sufficient length to be justly comparable, and in it the results of the experiments are divided into three groups. Group A comprises those in which the addition of alcohol to a diet of ordinary nutrients was accompanied by an increased elimination of nitrogen amounting to more than .5 gram per day. Group B includes those cases in which the addition of alcohol was without effect upon the nitrogen balance, or did not appear to change it more than .3 gram. Group C comprises the experiments in which the addition of alcohol was immediately accompanied by a diminished output of nitrogen. Class II. groups together the experiments with alcohol periods longer than six days, in the final days of which the protein protection was most clearly and conclusively shown.

The experiments of Group A are of especial interest in this connection, since they apparently show a definite disintegrating action of the alcohol. They are the only ones that we have been able to find in which the amount of protein thus broken down with alcohol apparently exceeded, by more than 0.1 gram of nitrogen per day, the amount broken down without alcohol. In two of these cases, viz., Clopatt's experiments and Neumann's first series, the loss of nitrogen on alcohol days exceeded that on alcohol-free days by an amount which was 2.0 grams in one case and .9 gram in the other. The third is Miura's first series, in which the difference amounted to .5 gram per day.

As has been already pointed out, there is nothing to show how much of this loss of nitrogen from the body may be due to the diuretic effect of the alcohol, nor how much of it to a change in the amount of nitrogen in the alimentary canal or to other disturbing causes. During these three experimental periods the total amount of this difference, which is taken as a measure of the katabolic action of the alcohol, was about 10 grams in Clopatt's case, 2.8 in Neumann's, and 1.5 in Miura's, so that Clopatt's experiment is the only one in which the difference seems large enough to be really significant.

In any event it would be going very far to attempt to base a physiological principle upon so small a number of comparative experiments with no larger differences in results. To the writer it seems that in view of the unavoidable irregularities in the nitrogen balance in such experimenting, these data are insufficient to demonstrate the disintegrating action of alcohol, but taken in connection with the need of an explanation for the occasional failure of alcohol to protect protein

they make the theory plausible. It is the only satisfactory hypothesis which has thus far been suggested. It is all the easier to accept because of the considerations that the breaking up of protein compounds in the body seems to be influenced, in some unexplained way or ways, by the nervous system, and this latter, in turn, is influenced by alcohol. In our own experiments, for instance, the excretion of nitrogen was apparently affected at times, and to a considerable extent, by the mental condition of the subject.

Fats vs. carbohydrates as protectors of protein.—In the treatise already referred to, Rosenfeld draws some interesting comparisons between Miura's experiments with alcohol and Kayser's (78) experiments with fats replacing carbohydrates, and suggests that if Miura's results warrant calling alcohol a proteid poison, Kayser's would warrant the applying of the same term to fat. Rosemann objects to this on the ground that the experiments are not comparable, since in Kayser's experiments all of the carbohydrates were replaced by fat, so that in one period the diet consisted of protein and fats only.

It seems hardly probable that the fat in a diet would ordinarily tend actually to increase the katabolism of protein, and such an observed increase of nitrogen excretion might more naturally be ascribed to other causes. In some late experiments of our own, the details of which are soon to be published, in which large (isodynamic) amounts of fats and carbohydrates mutually replaced one another in the ration, the fats appeared to be in most cases decidedly inferior to the carbohydrates in protecting protein.

What Kayser's experiments and our own actually show is that the fat was inferior to the carbohydrates in protein protecting power. In the same way the experiments of Miura, Schoeneseiffen, Schmidt, Clopatt, Neumann, Rosemann, and some of our own, show that alcohol was inferior to carbohydrates and fats which it replaced. I am, however, aware of no instances in which the body lost more nitrogen with fat than without it. In the experiments above cited the only instances where it lost more with alcohol than without it are in the three mentioned (Miura, Clopatt, and Neumann), and the experiment of Clopatt was the only one in which the loss of nitrogen was considerable.

In discussing the protection of fat and of protein, it should be borne in mind that in a sense the two do not and cannot occur at the same time; in other words, the available energy of food and the amount of work done being equal, an increase in the katabolism of protein necessarily implies a corresponding decrease in the katabolism of fat or carbohydrates. The details of our own experiments show that where the alcohol was apparently less efficient in protecting protein it was at the same time more efficient in protecting fat.

In short, we have to do with a selective action in the body, by which in some cases more, and in others less proteid is katabolized. At the same time there is a corresponding change in the metabolism of fats and doubtless of other material, as glycogen, in the body. The factors which influence this selective action, and decide the amount of metabolism of proteids or other materials, are at present unknown. Their discovery is made all the more difficult by the numerous sources of error in such physiological experimenting. These and other considerations, too detailed for discussion here, call for great caution in drawing sweeping conclusions regarding the effect of alcohol either upon the protection or the disintegration of body protein.

Sources of uncertainty in this kind of experimenting.—One point which has hardly received the attention it deserves in discussions of this kind is the uncertainty of the nitrogen balance in any given case as a measure of the actual influence of a given condition upon nitrogen metabolism. This has been emphasized elsewhere in the present report (see page 252). Differences which look large in a table of figures are often far inside the unavoidable variations in actual experimenting.

Even when the differences are significant the interpretation may be erroneous. A striking illustration of the danger of such error is found in the current discussion of the question we are now considering. For a number of years past, writers upon this subject have insisted most positively that alcohol, instead of being a protector of protein, is a protein poison. This theory is based almost wholly upon the experiments of Miura, Schmidt, and Schoeneseiffen. The experiments of Neumann, Rosenfeld, Chotzen, Clopatt, and Rosemann, not to speak of others, including our own, have shown that this theory was wrong, and have given us a very plausible hypothesis to explain why it was wrong.

One cannot insist too strongly upon the danger of drawing positive conclusions from figures for nitrogen balance as a measure of protein protection by either alcohol or sugar or starch or fat. Certainty comes only with careful planning and execution and manifold repetition of experiments.

Incidentally it is to be noted that the excretion of nitrogen in the urine is not necessarily an exact measure of the amount of protein broken down in short periods, since the time between the disintegration of the protein and the appearance of the nitrogen in the urine, the so-called nitrogen lag, varies widely. The longer the experimental period the less the error from this source.

Finally there is the unsettled question as to how much of the protein metabolized is that of food and how much comes from organized tissue.

Utilization of alcohol by invalids and by habitual users. — It is a common observation of physicians that in certain forms of disease in which the bodily activities are at a low ebb, alcohol may be administered with advantage; that patients in such circumstances show every indication of receiving actual nourishment from it; and that they often take, without intoxicating effect, quantities which would, under ordinary circumstances, produce drunkenness. It is also a matter of not infrequent observation that people not suffering from acute disease and taking alcohol habitually may use only very small quantities of ordinary nourishment.

The following illustration of the nourishing effect of alcohol in sickness is taken, with slight verbal changes, from a personal letter of Dr. S. L. Abbot to Prof. H. P. Bowditch of the Harvard Medical School, who has kindly permitted its use here. It relates the experience of Dr. Abbot with a patient in the Massachusetts General Hospital: —

“The patient was a young, very good-looking girl who entered the hospital very ill with double pneumonia, both lungs being solidified below the scapula. She was so very sick that she was put in ward 24, one of the long, one-story wards, cut up into small rooms, so that each patient might be by himself. My house-student told me he could not get her to swallow anything of a quieting nature; in fact she would swallow nothing. She was evidently mildly delirious, quiet, with a quick, feeble, irregular pulse and short, embarrassed breathing. When I spoke to her she gave me no answer. She made no complaint. I asked my assistant to bring me some milk. I presented a teaspoon of it to her lips, and she immediately clicked her teeth and tried to turn her head away so as not to swallow a drop of it. I did not care to use any force in such a case, and so did not urge her any further. I then told my assistant to bring me some brandy. I mixed a little of it with water in a teaspoon and presented it to her lips. A drop or two got into her mouth, and she did not reject it, but took the whole of it without any difficulty. I saw I had my cue. I directed the nurse to give her as much brandy and water as she would take, carefully watching for any signs of over-stimulation, and stopping if such indications appeared. The nurse’s report the next morning was that she had taken *half a bottle* of brandy without any unpleasant effects, and nothing else. She had slept very little, as had been the case for several nights. My order was, ‘Continue treatment.’ The next morning the report was a quiet night, with very little sleep. She had taken in twenty-four hours another pint of brandy. The same order, ‘Continue treatment,’ was given. The report on the third day was the same. The patient had slept more and was evidently doing well. The

order to continue treatment was repeated, but as the patient was drinking the most expensive French brandy I felt justified in changing the stimulant to Bourbon whiskey, which was considerably cheaper. On the fourth morning the nurse reported that 'three quarters' of a bottle of Bourbon whiskey (or a pint and a half of the liquor) had been taken in twenty-four hours, without any unpleasant effect, and the patient was sleeping better. And so it went on for the remaining three days in the week, the patient having a pint and a half of whiskey each twenty-four hours, with excellent effect. She was sleeping much better, had little or no fever, and a good pulse. On the morning of the eighth day the patient absolutely refused to take any more stimulant and began to take suitable food. Her convalescence was rapid and she got entirely well. During her illness she had during the critical week absolutely no food except what she got from stimulants, which I had reason to believe she had never tasted in her life before. In all, during the seven days, she had *nine pints or a gallon and a pint* of stimulant, and no other medicine."

The composition of whiskey is variable, but if we allow the pint to weigh 410 grams and to have 40 per cent. of absolute alcohol, the daily amount taken by this young woman, who was otherwise unaccustomed to the use of alcoholic beverages, would be 211 grams. This would have a fuel value of about 1456 calories, more than one half as much as would be contained in the ordinary food required by an average woman in health and engaged in light work, and fully as much as is contained in the daily diet of many women in poor health and without occupation.¹ That so large a quantity, taken with no other food, should produce no symptoms of intoxication and at the same time prove so efficient for sustenance, is certainly significant, the more so because it is not an isolated but a typical case.²

Among other cases exhibiting this remarkable tolerance for alcohol in disease are those described by Runge,³ in which use was made of alcohol in nine cases of women with puerperal fever, who received alcohol amounting to from 2.8 to 7.0 cc. per kilo body weight per day, during periods ranging from six to twenty-two days. All but two recovered. One of the patients, who was otherwise a total abstainer,

¹ The diet of infirm females in two New York hospitals for the insane was found to supply on the average 1570 calories per day. See page 239, *Second Report on Dietaries for Hospitals for the Insane in the State of New York*, by W. O. Atwater, in the *Eleventh Annual Report of the New York State Commission in Lunacy*. (Albany, N. Y., 1900.)

² See statements by Dr. F. C. Shattuck, *Boston Medical and Surgical Journal*, vol. cxlvi. No. 11, p. 279.

³ Quoted by Rosenfeld, *Alkohol und Organismus*, p. 162.

received alcohol for seven days at the rate of 7 cc. per kilo per day, and with great benefit. Assuming the body weight to have been 55 kilos (121 pounds), the daily amount of alcohol would have been 305 grams, with a fuel value of 2150 calories.

In his treatise on *Stimulants and Narcotics*¹ (pp. 432-465), Dr. F. E. Anstie treats of this subject in detail, basing his statements upon his own observations. He says:—

“By far the most important aspect, however, of the non-narcotic action of alcohol is that which is presented to us by the singular cases, which, however they may have been discredited, certainly do occasionally present themselves, of individuals subsisting for considerable periods of time without, or nearly without, other subsistence than alcohol, and yet escaping the prostration which entire starvation for a similar period would undoubtedly produce. The facts of this kind may be divided into two groups: (1) Those which concern the support of the organism in acute disease. (2) Those which concern the maintenance of bodily vigor upon an extremely insufficient allowance of ordinary food in a state of ordinary health.

“(1) As to the support of the organism (by alcohol) during the progress of acute disease, it is not disputed by those who have given a proper trial to the treatment that, in the partial or total absence of the power to take other food, patients in typhus, pneumonia, etc., frequently maintain vital power and preserve their intellectual faculties throughout, and on the termination of the severe symptoms of the disorder convalesce with remarkable rapidity. . . .

“(2) Passing from this subject, we have to consider the extraordinary way in which the healthy system (using this word comparatively) adapts itself, in some cases, to a diet composed chiefly, or almost entirely, of alcohol.”

Dr. Anstie cites a considerable number of cases under each of the two categories, *i. e.* (1) persons suffering from acute disease, as typhoid pneumonia, erysipelas, bronchitis, etc., and (2) habitual toppers, giving detailed descriptions and statistics of the age, sex, and habits of the subject, the nature of disease, or the habits of the inebriates, the length of the period during which the observations continued, the kinds and amounts of alcoholic liquors ingested, the ordinary food, when such was eaten, and the results as judged from the standpoint of the physician. One of the cases is thus described:—

“The case which first attracted my attention to the possibility of the human organism subsisting, under certain circumstances, for a long time upon alcohol only (or practically so), was that of an old man who became my patient in 1861 at the Westminster Hospital; he was

¹ London: Macmillan & Co. 1864.

at that time eighty-three years old, and was half led, half carried to the hospital by his daughter for relief from chronic bronchitis, which was just then severely aggravated. It happened that in prescribing for him, the subject of stimulants was mentioned, and the old man, apprehending that as a matter of course I should put him on a severe *régime* (he was an old soldier), begged and prayed that his 'drop of drink' might not be taken away from him. I somewhat carelessly inquired what the amount of the said 'drop' might ordinarily be, and received the astonishing answer — 'A bottle of gin a day.' Here the daughter interfered, and remarked that it would be the death of him to take away this source of support, for he ate no food. Inquiring what 'no food' meant, I was assured, again and again, that one small finger-length of bread, usually toasted, was all that he ever took from one end of the day to the other; he was occasionally drunk, but not often, and was a man of astonishingly active habits for his age. I need hardly say that it was a matter of utter impossibility for me to watch this man and his friends day and night to make sure that they were not deceiving me; but their story was confirmed by a neighbor who brought the old man on one occasion. I kept this case in view for a twelve-month, when a renewed access of bronchitis carried the patient off. Again I made searching inquiries, and was assured that the man's habits of life were such as I have mentioned, and that they had been so for a great number of years, about twenty years his daughter believed. It was certain that he did not take tea or coffee, or anything of that kind even; and the only thing besides his gin and water (which he drank unsweetened) which could have helped to support him was the daily fragment of bread and a few pipes of tobacco. His very expensive manner of living prevented his friends, who otherwise seemed decent folk, from affording paid medical advice. The man's appearance was very singular and not easy to describe; it was not that he was very greatly emaciated, but he had a dried-up look which reminded me of that of opium-eaters."

As Dr. Anstie himself insists, these observations lack the accuracy and completeness needed for absolute scientific demonstration; but a number of cases were those of patients in hospitals when the diet was definitely known and controlled, so that the fact of subsistence for periods covering several days or weeks with little or no ordinary food was definitely proven, and in the other cases the evidence was such as to leave little room to question its reliability. With such data, confirmed by many other reliable observers, it seems hardly possible to deny that, somehow, the body is able to derive nourishment from alcohol.

From the standpoint of the physiological chemist, this effect of

alcohol would seem entirely natural. The bodily functions are weakened, and the power of digestion is impaired. While the patient is lying still, the labor required of the muscles is not large, and the chief need is fuel to carry the body through the time of stress. What is wanted is a material which is easily tolerated, will not have to be digested, can be easily absorbed, is readily oxidized, and will supply the requisite energy.

I know of no other material, unless it be a monosaccharide like glucose, which would seem to meet these requirements so naturally and so fully as alcohol. It does not require digestion, is easily taken, is absorbed by the stomach, and presumably by the intestine, with great ease. Outside of the body it is oxidized very readily, within the body it appears to be readily burned, and it supplies a large amount of energy. Why it should have less effect upon the nervous system in some forms of illness than in health is perhaps hard to say, but that it should under these circumstances be an invaluable source of energy is easy to believe.

Summary and conclusions.

The inferences which may be legitimately drawn from the experiments above cited would seem to be :—

(1) The protection of protein by alcohol was evident in quite a number of cases. Either this did actually occur, or disturbing influences must have been efficient to an extent which we should hardly feel warranted in assuming. The number and variety of experiments in which the protein protection is manifest seem to warrant the general conclusion that alcohol can and sometimes does protect protein. This was the more evident and certain in experiments with long alcohol periods, and when the protecting action of alcohol was once established, it continued as long as the experiment lasted.

(2) The instances where alcohol failed for a time to protect protein are also numerous, but are limited to experiments with short alcohol periods or to the first four to six days of longer periods. The failure to protect protein is, in these cases at any rate, a temporary action which is not always manifested. The inference that alcohol *cannot* protect protein is therefore unwarranted because based upon insufficient experimental evidence.

(3) The hypothesis that alcohol may also tend to cause the disintegration of proteids is very plausible, and affords a simple explanation of the failure to protect, which has been observed in a number of cases, and of the increased excretion of nitrogen with alcohol over that without it, which was observed to a slight degree in the experiments of Neumann and Miura, and to a marked degree in those of Clopatt.

But these results are hardly sufficient to warrant the general conclusion that alcohol has a specific action in causing the disintegration of tissue proteid. That the action, if it exists, may be only temporary follows as a corollary to what has just been said regarding the failure of alcohol to protect protein.

(4) The data now available are not sufficient to define the relative capacities of sugar, fat, and alcohol for protecting protein. Their actual effect in a given case appears to be influenced by a number of conditions which are not clearly understood. Some apparently have to do with the personality of the individual and his mental or nervous condition, and some with the diet, including the order of succession of experimental periods. The available data, as a whole, would seem to imply that the carbohydrates are more efficient as protectors of protein than either fats or alcohol, and that as between the two latter, the difference is in favor of the fats.

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CHAPTER III.

EXPERIMENTS CONDUCTED UNDER THE AUSPICES OF THE COMMITTEE OF FIFTY.

Purpose of the experiments. The question stated.

THE main purpose of the experiments has been to get light upon the nutritive value of alcohol. The questions, as to whether alcohol is food, and whether and in what ways it supplies the body with nutriment, have been actively discussed for the last fifty years and more. No one doubts that the continued and excessive use of alcohol is injurious to body, mind, and character. No one questions that in large enough quantities it is really a poison. The debatable problem is its effect when taken in small or moderate quantities. The range of views among specialists as well as the public at large on this question is a wide one. At the one extreme are those who believe not only that it is a valuable nutriment, but that in small quantities, as used by those who drink their glass or two of wine, beer, or whiskey a day, it is healthful and useful and to be generally recommended even for persons in health. At the other extreme are those who urge that it has no nutritive value and is always poisonous, even in very small quantities. The great majority of physiologists and hygienists, it is doubtless safe to say, hold to the middle opinion that alcohol, taken in small quantities, may serve the body for nutriment, that it is at some times valuable, at others harmful.

To discuss the question properly, it must be subdivided. Ordinarily people take alcoholic beverages, not for the nutriment they contain, but for their pleasant taste and effects. The food value of alcohol must be considered apart from such ulterior effects, be they good or bad. Even the narrower question of food value must be subdivided before it can be answered clearly. We must distinguish between the different functions of food and inquire which ones alcohol does, and which ones it does not perform. We must also consider its indirect action,

as, for instance, in aiding or hindering the digestion of food and the various processes by which food is used by the body for its nourishment.

The two chief functions of food are to furnish materials for the growth and repair of the tissues and fluids of the body and to yield energy for maintaining the healthful bodily temperature and for its muscular work.

The first of these functions is performed mainly by the nitrogenous or protein compounds of food, the proteids. These are familiar to us in myosin or the lean of meat, in the casein (curd) of milk, the albumen or white of egg, and the gluten of wheat. The proteids yield energy ; but this function can be equally well performed by the other food ingredients, and the proteids are used primarily for the tissue building, which they alone can accomplish.

Thus the function of furnishing energy falls chiefly on the two remaining great classes of food ingredients, the fats and carbohydrates. The fat of meat, the fat of milk, which makes butter, and the oil of corn and wheat, are examples of fats. Starch, which is the principal ingredient of such foods as bread and potato, represents one class, and the sugars another class, of carbohydrates. These are burned in the body somewhat as coal is burned in the engine, and the energy which they yield in this oxidation is transformed into heat and muscular force. They are therefore called the fuel ingredients of food, and are said to have a high or a low fuel value according as they furnish much or little energy to the body. The fats and carbohydrates cannot build nitrogenous tissue, since they have no nitrogen ; accordingly they cannot take the place of the proteids as material for building and repair, although the proteids can to a greater or less extent do the work of the fats and carbohydrates in serving as fuel.

All three classes of nutrients can be stored in the body and held for future use. The proteids of the food may be transformed and stored as body proteid, or converted into body fat and stored as such. The fat of the food may be transformed and stored as body fat. The carbohydrates of the food may be converted into fat in the body and stored as body fat. These stored materials may be drawn upon by the body and used to supplement the energy of the food whenever the available

energy of the food is not sufficient for the demands of the body.

Alcohol contains no nitrogen and therefore cannot build or repair tissue ; it is rather to be classed with the fats and carbohydrates, and if it has any value, this must be a fuel. It does not appear to be stored for any considerable time, but it is disposed of soon after it is taken into the body.

Pharmacodynamic vs. nutritive action of alcohol.

Alcohol, however, differs from ordinary food materials and their nutritive ingredients in that it may exert, and, when taken in large enough doses, does exert an important influence upon the brain and nerves and through them upon the nutrition and other processes to which the general term metabolism is applied. In this way its value either may be increased, as in aiding digestion, or it may be more or less completely neutralized, as when it hinders digestion, or either accelerates or retards metabolism. We have then to consider not only its direct action as nutriment, but also its indirect action upon the metabolism and utilization of other food. In the experiments here described the indirect action of alcohol has been studied only in so far as (1) through its influence upon the secretion of digestive juices or otherwise it may have tended to increase or diminish the proportion of the other food digested, or (2) it has increased or decreased the metabolism of other food or body material.

The ulterior effects of alcohol do not come within the scope of this particular inquiry, which is limited to its use by the body as nutriment.

The question actually studied.

It appears, then, that the chief value of alcohol for nutriment must depend upon its service as fuel for supplying energy to the body. Accordingly the main question proposed for study was this : What is the value of alcohol for fuel, and how does it compare in this respect with sugar, starch, fats, and other nutriments of ordinary food materials ? A collateral question was the effect of alcohol upon the proportions of nutrients digested from the food with which it was taken.

Experimental research has shown several ways in which the ingredients of ordinary food and body material serve as fuel : they are oxidized in the body ; in the oxidation, their potential

energy becomes kinetic and is thus made useful to the body; part of this kinetic energy appears as heat; another part appears as muscular work; in yielding energy by its own oxidation, food protects the material of the body and of other food from consumption. We have then to consider how alcohol compares with the ordinary fuel ingredients of food in these ways.

It is clear that the main problem is that of the metabolism of energy in the body. In studying it we go down to the fundamental principles of physiology; indeed, to one of the foundations of material science.

The fundamental question is this: Is the energy of alcohol transformed like that of ordinary food materials?

The transformations of energy in the body. Conservation of energy.

In its material manifestations life consists of transformations of matter and energy. The plant gathers the elements it needs from soil and air, and builds them into its own substance. It does so "by grace and bounty of the sun," whose energy enables the plant to do the building and is stored in the substance of the plant. The ox eats the grass and transforms it into flesh, which makes our meat. We gather the wheat and make bread. We eat the bread and meat; their substance forms our bodies, and the energy which comes from the sun becomes our energy for bodily warmth and work.

Two great laws govern the material world, the laws of the conservation of matter and of energy. In accordance with these laws matter and energy can be transformed, but they cannot be either created or destroyed by means known to man. Ever since the law of the conservation of energy was propounded, men of science have believed that the living organism must be subject to it, but the absolute demonstration has been lacking. The research by which this must be proved, if proven at all, is laborious and costly. Some late experiments, however, have, it is safe to say, shown that the law does hold in the living organism; that when the energy of the food is transformed in the body, the income and outgo are the same. The experiments are made by measuring the material which the body burns, determining how much heat it would yield if burned

directly with oxygen outside the body, and then finding just how much energy is produced when it is burned in the body. The first experiments in which a balance of income and outgo of energy was obtained, were made with dogs by Professor Rubner at the University of Erlangen in Germany a dozen years ago. The dogs did no (external) muscular work, and the amounts of material burned in the body were partly measured and partly calculated. The quantity of heat given off from the body was measured and found to agree very closely with the heat of oxidation — that is, the potential energy of the material estimated to be burned in the body.

Within the past four years much more elaborate series of experiments with men have been made by the writer and associates in the chemical laboratory of Wesleyan University. The quantities and potential energy of the materials burned in the body have been measured, as has also the energy given off from the body in the forms of both heat and muscular work. The agreement between the potential energy (heat of combustion) of the material oxidized in the body and the kinetic energy given off from the body in the forms of heat and (the heat equivalent of) external muscular work was so close as to imply that practically all the energy of the material burned in the body was transformed into measurable kinetic energy in accordance with the law of the conservation of energy.

The experiments are made with an apparatus called a respiration calorimeter which was especially devised for research of this kind and was used for the experiments on the nutritive value of alcohol. The apparatus serves to measure the materials received and given off from the body, including the products of respiration, and is thus a "respiration apparatus." It also serves to measure the heat given off by the body, and hence is a form of calorimeter. To indicate this twofold purpose it is called a "respiration calorimeter." As accounts of this apparatus and of the methods and results of experimenting with it have been published in detail elsewhere,¹ a brief description will suffice here.

¹ In the following bulletins of the Office of Experiment Stations of the United States Department of Agriculture: No. 44, *Report of Preliminary Investigations on the Metabolism of Nitrogen and Carbon in the Human Organism with a Respiration Calorimeter of Special Construction*, by W. O. Atwater,

The respiration calorimeter and methods of experiment.

The apparatus includes a copper walled chamber about seven feet long, four feet wide, and six and one half feet high, in which the man who serves as subject of the experiment lives during a period of four to twelve days and nights. An opening in the front of the apparatus, which is sealed during an experiment, serves as both door and window, and admits ample light for reading or writing. A smaller opening in the rear of the apparatus, called the food aperture, having tightly fitting caps on both ends, is used for passing food, drink, excreta, and other materials into and out of the chamber. There is a telephone by which the subject may communicate with those outside. The chamber is furnished with a chair, table, and bed, each of which may be folded up and set aside when not in use. A stationary bicycle is also supplied when the subject is to do muscular work during the experiment. Air is kept in circulation through the chamber at the rate of not far from two and a half cubic feet a minute. Thus, while the dimensions of the chamber are rather small, the subject finds nothing particularly disagreeable or uncomfortable in his sojourn within it, save for the restricted space and the monotony of the prescribed daily routine. But so little are these felt that each of the five men who have thus far sojourned in the calorimeter has found it a very tolerable place of residence and has been perfectly willing to repeat the experience. It may therefore be considered that the conditions are not sufficiently abnormal to affect the results of the experiments. This is an important consideration.

The circulation of air is effected by a special pump, which measures the volume of the ventilating current, and at regular intervals draws measured samples of the outgoing air for analysis. At the same time samples of the incoming air are also taken for analysis. From these determinations the amounts of respiratory products — carbon dioxide and water — given off by the subject may be computed.

Heat is constantly given off within the chamber by the man's body, whether he is at work or at rest. When he is at rest, *i. e.* doing no

Ph. D., C. D. Woods, B. S., and F. G. Benedict, Ph. D.; No. 63, *Description of a New Respiration Calorimeter and Experiments on the Conservation of Energy in the Human Body*, by W. O. Atwater, Ph. D., and E. B. Rosa, Ph. D., pp. 94; No. 69, *Experiments on the Metabolism of Matter and Energy in the Human Body*, by W. O. Atwater, Ph. D., and F. G. Benedict, Ph. D., with the coöperation of A. W. Smith, M. S., and A. P. Bryant, M. S., pp. 112; No. 109, *Experiments on the Metabolism of Matter and Energy in the Human Body*, 1898-1900, by W. O. Atwater, Ph. D., and F. G. Benedict, Ph. D., with the coöperation of A. P. Bryant, M. S., A. W. Smith, M. S., and J. F. Snell, Ph. D.

external muscular work, there is nevertheless a great deal of muscular work going on within his body. Even when he is asleep the organs of respiration, circulation, and digestion are active. The energy of the internal work is transformed into heat in the body and leaves the body as heat. This is proven by the fact, explained beyond, that when the body is at rest the heat it gives off is equal to the potential energy (heat of oxidation) of the material oxidized in the body.

When the man is working the bicycle, part of the power which he applies to the pedals is transformed into the heat of friction of the machine, but the larger part is transformed into electrical energy by means of a dynamo connected with the bicycle. The electrical current, thus produced by the bicycle-dynamo, passes through a lamp and is changed into heat. In this way all of the external muscular work done, *i. e.* all the power applied to the pedals, is transformed into heat within the chamber. Arrangements are made for measuring the heat of friction and also the electrical current produced by the bicycle-dynamo. The latter therefore serves as an ergometer for measuring the external muscular work.

We warm our houses in winter by a current of hot water which passes through radiators by which the heat is radiated into the rooms. We may hereafter learn to cool them in summer by the opposite process, *i. e.* by passing cold water through the pipes and making them absorbers, so that the water will carry away the heat. Precisely this is done in the respiration calorimeter. A copper pipe passes around the chamber close to the walls; through this flows a current of cold water, and by regulating the temperature and rate of flow of the water current, the heat is absorbed and carried out of the chamber as fast as generated. The temperature within the chamber is thus kept at a point agreeable to the subject and remains almost absolutely constant — indeed, the variations are often within a single degree during the whole twenty-four hours.

The diet during the experiment is uniform from day to day. All food and drink passed into the chamber, and all solid and liquid excreta passed out are carefully weighed, sampled, and analyzed. By comparing the chemical elements and compounds received by the body in food, drink, and inhaled air with those given off in the solid, liquid, and gaseous excretions from the body, it is possible to strike a balance between the total income and the total outgo of matter in the body, and to determine whether it has increased or diminished its store of material. In this way a gain or loss of even a small fraction of an ounce of body fat or protein during a period of one or several days can be detected and measured.

The above indicates the method of investigating the metabolism of

matter in the body. It consists practically in measuring the income and outgo of matter and striking the balance between the two. At the same time it is desirable to study the metabolism of energy. This is done likewise by determining the balance of income and outgo. The measurements made in these investigations are in terms of heat, since other forms of energy may be transformed into heat. To this end it is necessary to know how much energy is taken into the body in food and drink, how much is given off unused in the solid and liquid excreta, and how much is transformed in the body and given off in the forms of heat and external muscular work.

So far as we now know the only energy received by the body is the potential energy of the food, and the only forms in which it leaves the body are (1) partly in the potential energy of the unoxidized residues of food and body material which are eliminated in the solid and liquid excreta, but (2) chiefly in the kinetic energy resulting from the oxidation of material in the body.

The only forms in which kinetic energy is known to leave the human body are heat and external muscular work. Some animals, as the electrical eel, can give off small amounts as electrical energy; others, as the firefly, emit minute quantities as light, but they are exceptional. It has been surmised that mental work and nervous tension may represent forms of physical energy analogous to light, heat, and other forms now known, just as the X-ray represents a form of energy unknown until a few years ago. But there is no experimental proof for this theory, and it is opposed by the fact, explained beyond, that the energy given off from the body in the forms of heat and external muscular work is found to equal the potential energy of the materials oxidized in the body.

The potential energy of the food and excretory products is measured by the amount of heat generated when these substances are burned outside the body, that is by their heats of combustion, as learned by burning them with oxygen in an apparatus called the bomb calorimeter. The measurements of the kinetic energy given off from the body are made by means of the respiration calorimeter. The principle used in the measurement of energy by the respiration calorimeter is this. In the rest experiments, practically all the kinetic energy leaves the body as heat. In the work experiments part is put forth as muscular power applied to the pedals of the bicycle-dynamo, which transforms this external muscular energy into heat, and, as an ergometer, measures its amount. The problem is to measure the whole heat including that which left the body as heat, and that which resulted from the transformation of the energy of the external muscular work. The measurement is made in the following manner :—

The chamber of the calorimeter is inclosed by double metal walls, which are surrounded on all sides by walls of wood with air spaces between, so that the temperature within the chamber is not greatly affected by the changes in temperature of the room outside. Very delicate electrical devices show changes in temperature of the metal walls; and devices for heating and cooling the walls are arranged so that their temperature may be kept as near that of the interior of the chamber as desired, and the very small amounts of heat that may pass through them into or out of the calorimeter may be made to counter-balance each other. The temperature of the ventilating air current is also regulated, so that neither more nor less heat is taken in than is brought out. Accordingly there is no gain or loss of heat either through the walls of the chamber or by the ventilating air current. The heat produced within the chamber is that from the energy of the material oxidized in the man's body. The only way this heat can escape is by the proper agencies for carrying it out and measuring it.

These agencies are two, water vapor and the cold water current. About one fifth portion of the heat generated within the chamber is carried out by water vapor in the ventilating air current. The excess of vapor in the air that leaves the chamber over that in the air that enters it represents water which has been given off as vapor from the body of the subject, and has required heat to vaporize it. The amount of heat thus carried out of the chamber is computed from the amount of water vapor and the temperature at which it leaves the chamber.

The larger part of the heat generated within the chamber is absorbed and carried out by the current of cold water, above referred to as flowing through a copper pipe around the interior of the chamber. The cooling surface of the pipe is increased by thin disks of copper fastened at close intervals along the coil. The water enters the chamber at a low temperature, passes through the copper coil, absorbs heat from the chamber, and passes out at a higher temperature. The quantity of water that passes through the coil, and the difference between the temperatures at which it enters and leaves the coil are carefully determined, and show how much heat was thus brought out of the chamber. Adding the heat brought out by the water vapor in the ventilating air current to the heat brought out by the water current, we have the whole heat produced in the chamber. This is the measure of the kinetic energy which resulted from the oxidation of food and body material in the man's body. In other words, it is the energy which he transformed, or, to use another expression, it is the measure of the metabolism of energy in his body.

So delicate are the measurements of temperature of the air within the chamber, and of the metal walls, that the observer sitting outside

the apparatus, and noting the changes every two or four minutes, immediately detects a rise or fall of even one one-hundredth of a degree. For instance, if the man inside rises to move about, the increase in the heat given off from his body with the muscular work involved shows itself in a rise of temperature, which the observer immediately detects.

To complete the records made by the observers, the subject himself keeps a diary in which he records periodical observations of his weight, pulse-rate, and axillary or sub-lingual temperature, together with any statements which may be of service in interpreting the results of the experiments.

The net income of energy of the body is computed from the energy of food, drink, solid and liquid excretory products, and body material stored or lost, an allowance being made for slight changes in temperature of the apparatus and the body during the experiment. The net outgo is measured by the apparatus. By comparing these the balance of income and outgo of energy is found.

The data for the metabolism of matter and of energy, obtained as explained above, taken in connection with what is known of the physiological processes that go on in the body, give more accurate information than can be otherwise obtained regarding the ways in which the food is used in the body, the quantities of different food ingredients that are needed to supply the demands of the body, the different conditions of rest and work, and the comparative nutritive value of different food materials.

The accuracy of the apparatus and methods.

Two methods of testing the accuracy of the apparatus are employed. By one method known amounts of heat are generated electrically within the chamber, and the heat is measured by the apparatus. In this way its accuracy as a calorimeter only is tested. By the second method known amounts of ethyl alcohol of known purity and composition are burned completely within the chamber, and the amounts of water, carbon dioxide, and heat resulting from the combustion of alcohol are determined by the apparatus. In this way its accuracy, both as a respiration apparatus and as a calorimeter, is tested. In the average of five electrical tests the amount of heat measured by the calorimeter was 100.01 per cent. of the amount generated by the electric current. The averages of the results obtained in seventeen alcohol tests are summarized in the following table: —

Summary of results in which alcohol was burned in the calorimeter.

	Carbon dioxide. Grams.	Water. Grams.	Heat. Calories.
Amount required	19,239.8	12,264.4	64,554.1
Amount found	19,206.9	12,379.1	64,513.3
Ratio of amount found to amount required	99.8%	¹ 100.9%	99.9%

The results thus indicate that the respiration calorimeter is an instrument of precision, and that the determinations of carbon dioxide, water, and heat produced within the chamber of the respiration calorimeter are sufficiently accurate for experiments with the living subject.

THE EXPERIMENTS.

General plan.

In the investigation here described, experiments with ordinary diet were compared with those in which part of the fats and carbohydrates of the same diet were replaced by isodynamic amounts of alcohol. That is to say, the man under experiment lived for a certain number of days upon ordinary food, such as had been found to be fitted to his needs, and the results were noted. Thereafter the experiment was repeated under essentially the same conditions, save that part of the fats and carbohydrates or both were removed and enough alcohol was added to supply the same amount of potential energy as was contained in the fats or carbohydrates which it replaced. Thus the amounts of protein and energy were the same or nearly the same in both experiments. A considerable number of such series of experiments were made with different men under different conditions of rest and work. In the discussion of these experiments in the following pages, the terms "ordinary diet" and "alcohol diet" are used for convenience in distinguishing between the diet consisting of ordinary food materials without alcohol and the diet in which a portion of the carbonaceous nutrients of the ordinary diet was replaced by alcohol.

The alcohol amounted in general to two and one half ounces a day,

¹ After the completion of the later experiments a slight leak was found in the "valve box" through which the outgoing air current passed on its way to and from the "freezers," and by which water, condensed on the outside, may have entered. There is every reason to believe that the quantity of water actually found was thus made too large by a fraction of 1 per cent. In the average of the first nine experiments the amount of water found was 100.6 per cent. of that required. As an alcohol check test was generally made between each two metabolism experiments or series of experiments, we have a means of knowing when the leak began to affect the results and the amount of the error introduced. See Bulletin 109 of the Office of Experiment Stations, above referred to.

or about as much as would be contained in a bottle of claret or three or four glasses of whiskey. In most cases pure (ethyl) alcohol, but in some whiskey or brandy was used. It was mixed with either water or coffee and was given in six small doses, three with meals and the rest at regular intervals between, in order to avoid any undue effect upon the nerves. The alcohol supplied not far from 500 calories of energy per day. In the experiments without external muscular work, the total energy of the daily diet was generally about 2500 calories, so that the alcohol furnished one fifth of the total energy. In the experiments in which the man was engaged in more or less active muscular work, the total energy of the food was larger, averaging about 3900 calories, so that the alcohol furnished between one seventh and one eighth of the total energy of the diet. Alcohol was thus used in thirteen experiments with three men. These have been compared with the same number of experiments with ordinary diet without alcohol, but furnishing nearly the same amounts of protein and energy.

For the subject of the experiments a man is selected who is in good health, has apparently normal digestion, and does not find the confinement in the chamber uncomfortable. The diet is made as varied and palatable as is consistent with convenient preparation and with accurate sampling and analysis of the several food materials used. The quantity and composition of the diet are generally such as to maintain the body nearly in nitrogen and carbon equilibrium under the conditions of the experiment, whether of work or of rest. In order that the subject may become accustomed to this diet and reach approximate nitrogen equilibrium with it before the experiment proper begins, a preliminary digestion experiment of three or more, commonly four days, immediately precedes the metabolism experiment. During the preliminary period the subject conforms his muscular activity more or less to that of the coming experiment. Thus, if it is to be a work experiment, he rides a bicycle or walks a considerable distance each day. If it is to be a rest experiment, he avoids all unnecessary exercise. For supper on the last day of this preliminary digestion experiment about .3 of a gram of lampblack is taken in a gelatin capsule with the food, in order to mark the separation of the feces of the preliminary experiment from those of the metabolism experiment proper. The subject enters the chamber about seven o'clock on the evening of the last day of the preliminary digestion period and retires about eleven o'clock. At about one o'clock in the morning the heat measurements are begun.

The night sojourn in the apparatus suffices to get the temperature of the apparatus and its contents of carbonic acid and water into approximate equilibrium, so that accurate measurements may begin at

seven o'clock on the first morning of the experiment proper. In some cases this experiment continues only four days, in other cases the experimental period consists of six or nine successive days spent within the apparatus, the entire period being divided into experiments of two or three days each with changes in the diet as hereafter explained. The determinations of carbon dioxide, water vapor, and heat are made in six-hour periods, so that complete data for an experiment show the total amounts of these compounds given off from the body during the periods ending at 1 P. M., 7 P. M., 1 A. M., and 7 A. M. of each day of the experiment. The urine is also collected and the nitrogen determined for corresponding periods.

The daily routine of the subject within the chamber is indicated by a programme that is made up before the beginning of the experiment. A copy of the programme is furnished to the subject, who follows it with reasonable closeness, and other copies are posted in convenient places outside the apparatus for the benefit of those who have the experiment in charge.

Much care is necessary in preparing the food materials selected for the diet and in taking samples for analysis. With the exception of milk and alcohol, the proper quantity of each kind of food, either for each meal or for the whole day, is put up in glass jars before the experiment begins; and materials which might spoil during the course of the experiment, such as bread and meat, are thoroughly sterilized. Then, as is frequently the case, a man has to spend nine days and ten nights in the chamber of the apparatus, and the food must be prepared in sufficient quantity not only for this period, but also for the preliminary digestion experiment of four days, with an allowance of extra amounts for analysis and for various contingencies; the number of jars of food to be put up is large. The portion of each of the food materials as meat, bread, breakfast cereals, butter, sugar, and the like, for each meal or each day must be weighed with care, so that the mere labor of putting the food in the jars is considerable. As samples must be subjected to chemical analysis, the special work of the analytical chemist is quite large also.

Special arrangements were made by which the mixed milk from a definite number of selected cows is supplied for each experiment. But even with this precaution the milk is not entirely uniform in composition from day to day.

The handling of the alcohol is a much simpler matter. A quantity sufficient for several experiments is analyzed and the proper amounts are drawn each day.

The analysis of air before and after it passes through the chamber, the handling of excretory products, and other details too numerous even

for mention here, are fully described in the publications referred to on pages 224 and 239.

Details of the experiments.

The details of the experiments include : —

1. Kinds of experimental data and methods for obtaining them.
2. Statistical details of metabolism experiments with alcohol.
3. Statistical details of digestion experiments with alcohol.
4. Tabular summaries.

Data. Experimental methods.

The larger part of the statistics of the metabolism experiments have to do with the income and outgo of material and energy.

Experimental data of income. — These include statistics of the kinds, amounts, composition, and potential energy of food and drink, the volume of the ventilating current of air entering the chamber, and the amount of carbon dioxide and water in that air.

Experimental data of outgo. — These include statistics of the amount, composition, and heat of combustion of the unoxidized materials of feces and urine, the quantity of carbon dioxide and water in the air leaving the chamber, and the total energy given off by the body in the form of heat and external muscular work.

Apparatus and general methods of inquiry. — The respiration calorimeter and method of its use have been described in detail in publications referred to on page 224. The methods of analysis of food, feces, and urine were, in the main, those adopted by the Association of Official Agricultural Chemists,¹ but with certain modifications which have been developed in this laboratory.² The heats of combustion were determined by use of the bomb calorimeter.³

Statistical details of experiments.

The details of the methods of conducting the experiments will be advantageously given in connection with the description of one of the experiments. For this purpose we select No. 12.

¹ See Bulletin 46, revised, of the Division of Chemistry, U. S. Dept. Agr.

² See U. S. Dept. Agr., Office of Experiment Stations, Bull. 44, p. 22; Bull. 69, p. 18; and Report of Storrs (Conn.) Exp. Sta. 1891, p. 47. The methods for the determination of carbon and hydrogen in use in this laboratory are described in detail by F. G. Benedict in *Elementary Organic Analysis*, The Chemical Publishing Co., on page 51 of which the apparatus is pictured.

³ The bomb calorimeter and accessory apparatus used have been described by W. O. Atwater and associates in Bulletin 21 of the Office of Experiment

Experiment No. 12 — work with alcohol diet.

Subject. — E. O., laboratory assistant, 31 years of age, and weighing, without clothing, about 71 kilograms (157 pounds).

Occupation during experiment. — Work 8 hours a day upon a stationary bicycle belted to a small dynamo, thus making an ergometer as described on page 226. The voltage was measured and the current passed through resistance within the apparatus and thus transformed into heat and measured with the heat given off by the subject. Previous calibration showed the amount of work done in driving the bicycle.

Duration. — Preliminary period 4 days, beginning with breakfast, April 8, 1898, and experiment proper 4 days, beginning at 7 a. m. April 12, and ending at 7 a. m. April 16. The subject entered the respiration chamber on the evening of April 11, and thus spent 5 nights and 4 days within the calorimeter.

Diet. — Ordinary food furnishing 121 grams of protein and 3379 calories of energy, and in addition 72.4 grams of alcohol, furnishing 512 calories of energy, making the total energy of the diet 3891 calories. The alcohol was added to a sweetened coffee infusion. It was taken in 6 doses, 3 with the meals and the other 3 between meals and just before retiring. The coffee infusion was prepared in the usual manner, care being taken to keep that given to the subject free from particles of coffee. To 690 grams of infusion were added 50 grams of sugar and 80 grams of commercial ethyl alcohol containing 90.63 per cent. absolute alcohol. The 80 grams of commercial alcohol thus contained 72.4 grams of absolute alcohol and 7.6 grams water. The diet was practically the same during both the preliminary digestion experiment and the metabolism experiment proper. The kinds and amounts of different food materials taken at each meal and the amounts of coffee infusion and water consumed at different times during the day are shown herewith.

Composition of coffee infusion. — Coffee infusion was prepared by pouring boiling water over ground coffee and straining the infusion thus obtained. The nitrogen was determined in this infusion and found to amount to about 0.004 grams per litre — a quantity too small to be taken into account. The coffee infusion is therefore reckoned simply as so much water.

Stations of the U. S. Dept. Agr., p. 123, and in the Reports of the Storrs (Conn.) Exp. Sta. 1894, p. 133, and 1897, p. 199.

Diet in metabolism experiment No. 12.

FOOD.

	Breakfast.	Dinner.	Supper.	Total.
	Grams.	Grams.	Grams.	Grams.
Beef	75	100	—	175
Deviled ham	—	—	50	50
Butter	25	40	30	95
Whole milk	250	260	390	900
Bread	75	100	125	300
Maize breakfast food	60	—	—	60
Sugar	20	—	150	170
Alcohol	—	—	—	² 72.4

DRINK.

Time.	Amount.	
	Coffee infusion with alcohol and sugar. ³	Water.
	Grams.	Grams.
Breakfast	175	200
10.20 a. m.	150	200
12.30 p. m.	—	200
Dinner	175	—
3.50 p. m.	125	200
Supper	175	—
10 p. m.	130	200
Total	930	1000

¹ Including 50 grams used in coffee infusion and alcohol.² Added to coffee infusion and taken as indicated below.³ Made by adding 80 grams of 90.5 per cent. commercial alcohol and 50 grams sugar to 800 grams coffee infusion. The mixture then contained 807.6 grams water, 72.4 grams absolute alcohol, and 50 grams sugar.

Daily routine.—The routine in experiment No. 12 was as follows:—

Daily programme — Metabolism experiment No. 12.

7.00 a. m.	Rise, pass urine, collect drip, weigh absorbers, weigh self stripped and dressed.	1.50 p. m.	Begin work.
7.45 a. m.	Breakfast, drink 200 grams water.	3.50 p. m.	Stop work, rest 10 minutes, drink alcohol, drink 200 grams water.
8.20 a. m.	Begin work.	4.00 p. m.	Begin work.
10.20 a. m.	Rest 10 minutes, drink alcohol, drink 200 grams water.	6.00 p. m.	Stop work.
10.30 a. m.	Begin work.	6.30 p. m.	Supper, change underclothes, weigh self stripped and dressed.
12.30 p. m.	Stop work, drink 200 grams water.	7.00 p. m.	Pass urine, collect drip, weigh absorbers.
1.00 p. m.	Pass urine, collect drip, weigh absorbers.	10.00 p. m.	Drink 200 grams water, retire.
1.15 p. m.	Dinner.	1.00 a. m.	Pass urine.

The subject weighed himself, with and without clothing, at about 7 a. m. and 7 p. m. each day of the experiment. He observed his pulse rate, after intervals of rest, and took his body temperature from time to time by means of a registered clinical thermometer. The body temperatures were measured *sub lingua*. We do not think that great reliance can be placed upon observations for either pulse rate or temperature when made by the subject upon himself under such conditions.

A hygrometer inside the chamber was observed two or three times each day in order to give data concerning the amount of water vapor within the calorimeter, but the figures are not used in the final computations of results.

These statistics noted by the subject within the calorimeter are recorded in a diary, together with any other information which he thinks may be of value in interpreting the results of the experiment.

The main facts in the diary of experiment No. 12 are shown in the table herewith.

Summary of diary — Metabolism experiment No. 12.

Date and time.	Weight of subject.		Pulse rate per minute.	Temperature.	Hygrometer.	
	Without clothes.	With clothes.			Dry bulb.	Wet bulb.
	Kilograms.	Kilograms.		°F.	°C.	°C.
Apr. 12, 7.00 a. m. .	70.92	75.09	64	98.4	21.5	16.4
12, 12.40 p. m. .	—	—	68	98.8	21.8	18.6
12, 7.00 p. m. .	71.72	75.38	—	—	—	—
12, 9.45 p. m. .	—	—	77	98.3	21.5	18.0
13, 7.00 a. m. .	71.09	74.82	56	96.1	21.4	17.4
13, 12.40 p. m. .	—	—	68	98.8	21.5	18.8
13, 6.30 p. m. .	71.40	74.96	—	—	—	—
13, 9.45 p. m. .	—	—	71	98.4	21.5	18.0
14, 7.00 a. m. .	70.56	74.19	58	97.0	21.4	17.0
14, 12.40 p. m. .	—	—	70	99.0	21.4	18.8
14, 6.30 p. m. .	70.98	74.50	—	—	—	—
14, 9.45 p. m. .	—	—	73	98.5	21.5	17.8
15, 7.00 a. m. .	70.47	73.98	57	97.2	21.3	16.8
15, 12.40 p. m. .	—	—	72	97.0	21.7	19.0
15, 7.00 p. m. .	71.12	74.51	—	—	—	—
15, 9.45 p. m. .	—	—	74	99.0	21.5	17.8
16, 7.00 a. m. .	70.31	73.98	60	96.4	22.0	18.4

The principal statistics are given in tables the subjects of which are indicated by the following titles. The numbers are those of the tables in the memoir. Tables I., II., and III. give analyses of food materials and feces of this and other experiments. Table IV. is here quoted. The rest are :—

Table V. — Record of work done (on bicycle).

Table VI. — Weight, composition, and heat of combustion of foods.

Table VII. — Weight, composition, and heat of combustion of feces.

Table VIII. — Amount, specific gravity, and nitrogen of urine by 6-hour periods.

Table IX. — Daily elimination of carbon, hydrogen, water, and energy in urine.

Table X. — Comparison of residual amounts of carbon dioxide and water in the chamber at the beginning and end of each period, and the corresponding gain or loss.

Table XI. — Record of carbon dioxide in ventilating air current.

Table XII. — Record of water in ventilating air current.

Table XIII. — Summary of calorimetric measurements.

Table XIV. — Alcohol ingested and excreted.

Table XV. — Income and outgo of nitrogen and carbon.

Table XVI. — Income and outgo of water and hydrogen.

Table XVII. — Gain or loss of protein ($N \times 6.25$), fat, and water.

Table XVIII. — Income and outgo of energy.

The tables of this experiment with descriptive text fill 14 quarto pages. They are, however, much condensed. Thus the statistics of Table XIII., which fill less than three fifths of a printed page, are made up from heat measurements with the respiration calorimeter. The figures for these measurements for each hour of the day, as recorded, fill a note-book page about 9×12 inches, so that the notes for the 4 days of the experiment fill 96 note-book pages. During the progress of an experiment, ten men are steadily at work, two or three during the night, the rest during the day, but a considerable part of the labor precedes and much the larger part of the whole follows the experiment proper. Inasmuch as there is always the possibility that some part of the apparatus may get out of order during an experiment, — a leak, for instance, might occur and be unobserved, — the accuracy of its working is generally tested between each two series of experiments, by burning a known amount of alcohol in the chamber. Results of these alcohol check-tests are given in detail in the memoir, and are summarized on page 230.

The men who served as subjects of the experiments.

Three different men, E. O., A. W. S., and J. F. S., have served as subjects in these experiments. Each of these when not sojourning in the apparatus was engaged in work connected with the investigations. E. O. was a general assistant in the chemical laboratory, a Swede by birth, who had been a number of years in this country; he was 32–33 years old, and weighed about 155 pounds. Since boyhood he has been accustomed to the moderate use of alcoholic beverages. A. W. S. was a physicist, a native of New England, 25 years old, and weighed about 155 pounds. J. F. S. was a chemist, a Canadian by birth, 29 years old, and weighed about 150 pounds. Both of the last two had always been total abstainers.

Symptoms observed in experiments with alcohol.

In deciding upon the daily amount of alcohol and its division into doses, the purpose was to give the subjects as much as they could well take without apparent nervous disturbance. As above stated, the quantity of absolute alcohol, about 72 grams per day, was divided into six nearly equal doses, of which three were taken with the meals and three between meals. It supplied about one fifth of the total energy of the diet in the rest experiments and about one seventh in the work experiments. On one or two occasions J. F. S. experienced a slight tingling in the ears immediately after drinking of the alcohol. On one occasion A. W. S. thought he experienced a very slight dizziness. On one occasion E. O. complained of a slight feeling of dullness. Otherwise neither one was at any time aware of any especial effect of the alcohol upon the sensations in any way. With the exception of the tingling in the ears noticed by J. F. S., it is not certain that any of the symptoms referred to were due to the alcohol.

As regards the effect of alcohol upon the body temperature and pulse rate in these experiments there is little to be said. The only observations made were those by the subjects themselves, and the difficulty of accurately determining one's own normal pulse rate is well known. The observations of temperature were made with a clinical thermometer in the mouth or axilla by the usual method, which of course does not show the exact average internal temperature of the body. The data obtained with E. O. and A. W. S. were not sufficiently accurate and numerous to be decisive. The observations by J. F. S. were made at frequent intervals and with considerable care. The results imply a slightly decreased body temperature and increased pulse rate in the experiments with alcohol diet, but the differences are not large.

List of experiments with and without alcohol, and grouping for comparison.

Of the metabolism experiments with men in the respiration calorimeter thirteen had for one of their objects the study of the nutritive value of alcohol. These are compared with a like number made with the same men, but without alcohol in the diet. Table 1 gives a list of these twenty-six experiments, with grouping for comparison and references to publications in which the details may be found.

TABLE 1. — *List of the experiments, and grouping for comparison of results with and without alcohol.*¹

Group.	No.	Date.	Duration.	Subject.	Nature of the experiment.		Protein in food.	Energy in food.
					Rest or work.	Ordinary or alcohol diet.		
		<i>More strictly comparable.</i>	Days.				Grams.	Calories.
A	9	Jan. 10-14, 1898.	4	E. O.	Rest.	Ordinary.	119	2717
	10	Feb. 15-19, 1898.	4	do.	Rest.	Alcohol.	123	2097
B	24	Mar. 19-22, 1899.	3	do.	Rest.	Ordinary.	124	3061
	22	Mar. 13-16, 1899.	3	do.	Rest.	Alcohol.	124	3044
C	26	Feb. 14-17, 1900.	3	J. F. S.	Rest.	Ordinary.	100	2490
	28	Feb. 20-23, 1900.	3	do.	Rest.	do.	99	2489
	27	Feb. 17-20, 1900.	3	do.	Rest.	Alcohol.	99	2491
D	11	Mar. 22-26, 1898.	4	E. O.	Work.	Ordinary.	124	3862
	12	Apr. 12-16, 1898.	4	do.	Work.	Alcohol.	121	3891
E	29	Mar. 16-19, 1900.	3	J. F. S.	Work.	Ordinary.	100	3487
	31	Mar. 22-25, 1900.	3	do.	Work.	do.	100	3495
	30	Mar. 19-22, 1900.	3	do.	Work.	Alcohol.	99	3458
F	32	Apr. 20-23, 1900.	3	do.	Work.	Ordinary.	101	3487
	34	Apr. 26-29, 1900.	3	do.	Work.	do.	100	3493
	33	Apr. 23-26, 1900.	3	do.	Work.	Alcohol.	100	3486
		<i>Less strictly comparable.</i>						
G	13	Nov. 8-11, 1898.	3	E. O.	Rest.	Ordinary.	117	2596
	14	Dec. 20-24, 1898.	4	do.	Rest.	do.	94	2513
	7	June 8-12, 1897.	4	do.	Rest.	Alcohol.	104	2462
H	5	May 4-8, 1897.	4	do.	Rest.	Ordinary.	119	2655
	15	Jan. 16-18, 1899.	2	do.	Rest.	Alcohol.	109	2653
	16	Jan. 18-20, 1899.	2	do.	Rest.	do.	109	2653
	17	Jan. 20-22, 1899.	2	do.	Rest.	do.	109	2653
I	21	Feb. 12-15, 1899.	3	A. W. S.	Rest.	Ordinary.	97	2264
	18	Feb. 6-8, 1899.	2	do.	Rest.	Alcohol.	97	2776
	19	Feb. 8-10, 1899.	2	do.	Rest.	do.	97	2776
	20	Feb. 10-12, 1899.	2	do.	Rest.	do.	97	2776

¹ The details of Nos. 5, 7, 9, and 10 are given in Bulletin 69 of the Office of Experiment Stations; those of Nos. 11, 13, 14, 21, 24, 26, 28, 29, 31, 32, and 34 in Bulletin 109 of the same office, and those of the rest in *Memoirs of the National Academy of Sciences*, vol. viii., Sixth Memoir, "An Experimental Inquiry regarding the Nutritive Value of Alcohol, by W. O. Atwater and F. G. Benedict: Washington: Government Printing Office, 1902."

The experiments are divided into groups, each group including experiments with and without alcohol, but made with the same subject. In some groups there are only two experiments, one with alcohol and one with ordinary diet; in others there are more than one experiment either with or without alcohol.

More and less strictly comparable experiments. — In the first six groups, A to F, inclusive, the experiments with and without alcohol were practically duplicates in duration, muscular activity, and amounts of protein and energy in the diet, the main difference being that a part of the fats and carbohydrates of the ordinary diet, enough to supply in general about 500 calories of energy, was replaced by the iso-

dynamic amount of alcohol. In the three groups, G to I, which include a number of the earlier experiments, those with and without alcohol were not so nearly duplicates. In some instances the difference was unintentional, and was due to a difficulty in obtaining food materials of like composition at different times. In these cases it was not found practicable to complete the analyses long enough in advance of the experiments to insure uniformity of diet as regards amounts of protein and energy. Later, means were devised for putting up food materials in considerable quantities and preserving them by canning or cold storage, so that the amounts of protein and energy in the diet were made more nearly the same in experiments separated by longer or shorter intervals of time. Accordingly the experiments of groups A to F are designated as more directly comparable and those of Groups G to I as less directly comparable.

DISCUSSION OF THE RESULTS OF THE EXPERIMENTS.

The special purpose of the experiments here summarized, in so far as they have had to do with the nutritive action of alcohol, has been the study of the metabolism of the energy of alcohol and its consequent value for fuel, especially as compared with isodynamic amounts of the ordinary fuel ingredients of food — carbohydrates and fats. Incidentally, its effects upon digestion, the completeness of its oxidation, and its action in protecting body fat and protein from oxidation have also been observed. The more important results may be discussed under the following topics:—

1. Effect of alcohol upon the digestion of food.
2. Proportions of alcohol oxidized and unoxidized.
3. Metabolism of the energy of alcohol.
4. Protection of body material by alcohol.
 - a. Protection of body fat.
 - b. Protection of body protein.
5. Effect of alcohol upon the radiation of heat from the body.
6. Rapidity of combustion of alcohol in the body.
7. Alcohol as a source of heat in the body.
8. Alcohol as a source of muscular energy.

Effect of alcohol upon the digestion of food. Digestibility vs. availability of nutrients.

The term digestibility as applied to food has several meanings which are not clearly distinguished in popular usage. It commonly refers to either the ease with which given food material is digested, or the time required for the process, or the extent to which the material “agrees” or “disagrees” with different persons, or its effects upon bodily com-

fort and health. These factors depend largely upon individual peculiarities, vary widely with different persons and with the character of the food, and are difficult to measure.

The term digestibility is also used to designate the quantity or proportion of the food or of each of its different ingredients — protein, fats, carbohydrates, and mineral matters — actually digested and absorbed in the passage of the food through the digestive tract. Only this latter factor of digestibility is considered in these experiments. To determine what amount of each nutrient is actually digested, it would be necessary to know the quantity that is taken into the body in food and the quantity that escapes digestion and is excreted in the feces. But the exact amount of this undigested residue is not easily determined because the feces contain, besides the portions of the food which have resisted the action of the digestive juices, certain other materials, called metabolic products. These latter, which are largely the residues of the digestive juices, are not easily separated from the undigested portion of the food. For this reason it is difficult to determine the actual digestibility of food and of its several ingredients.

The availability of the food and its several ingredients, however, may be more accurately determined. By availability is here meant the quantity or proportion that can be used for the building and repair of tissue and the yielding of energy. The metabolic products, although derived originally from the digested food, are not used for either building material or fuel, and hence are not available in the sense in which the word is here employed. They may therefore be included with the undigested residue of the food. The feces, which are made up of undigested food and metabolic products thus represent the unavailable material, and the amounts of available nutrients may be found by subtracting from the total ingredients of the food the total corresponding ingredients in the feces. These have often been called the digestible rather than the available nutrients, but the distinction here made is quite important. The availability of the ingredients as thus determined is usually expressed by the percentage of the total amounts of each in the food. This percentage is called the coefficient of availability. In like manner, the coefficient of availability of energy represents the share of the total energy which the body transforms. Thus it has been found that of every 100 calories of potential energy in the experiments with alcohol diet about 91 calories were changed to heat and external muscular work by healthy men; the coefficient of availability of the energy was accordingly 91 per cent. In Table 2, which is a summary of a more detailed table in the memoir referred to above, the coefficients of availability of the protein, fats, carbohydrates, and energy of the ordinary diet are compared with

those of the alcohol diet, as actually found in the experiments. The average coefficients of availability of the nutrients and energy of food, as found in 93 experiments with healthy men with ordinary diet under various conditions of work and rest,¹ are appended in the table for reference:—

TABLE 2. — *Coefficients of (digestibility) availability of food in the averages of experiments with and without alcohol.*

Kind and number of experiments.	Coefficients of availability.			
	Protein.	Fat.	Carbohydrate.	Energy.
	Per cent.	Per cent.	Per cent.	Per cent.
<i>Experiments more directly comparable.</i>				
Without alcohol, Nos. 9, 11, 26 and 28, 29 and 31, 32 and 34	92.6	94.9	97.9	91.9
With alcohol, Nos. 10, 12, 27, 31, 33	93.7	94.6	97.8	92.0
<i>Experiments less directly comparable.</i>				
Without alcohol, Nos. 5 and 13 and 14	92.6	94.1	98.1	90.3
With alcohol, Nos. 7 and 15 to 17 . .	95.0	94.4	98.3	91.3
Average of other observations . .	93.0	95.0	98.0	92.3

It thus appears that the alcohol had little appreciable effect upon the proportions of nutrients digested; the coefficients of availability of the nutrients of the ordinary food were very nearly the same with and without alcohol as part of the diet. The protein appears to have been slightly more available when the diet contained alcohol. The differences, especially in the more comparable experiments, are less than might be found with different subjects using the same ordinary food, or with the same subject using the same food at different times and under different conditions.

Conclusion.—The conclusion is that alcohol in moderate amounts tended to very slightly increase the digestibility of the protein, but did not materially alter the digestibility of the other nutrients. While such is the statistical result of these experiments, the extent to which it would be true in general experience is by no means certain. A natural inference is that like quantities of alcohol would not greatly affect the amounts of nutritive material digested from ordinary food by people in health. But it is to be remembered that these experiments give no test of the influence of alcohol upon either the completeness or the ease of digestion of food by people whose digestive powers are enfeebled.

¹ See Atwater and Bryant, "Availability and Fuel Value of Food Materials," *Report of Storrs (Conn.) Experiment Station*, 1899, p. 73.

Proportion of alcohol oxidized and unoxidized.

The difference between the amount of alcohol taken into the body in food and the amount given off unoxidized by the kidneys, lungs, and skin was taken as the amount oxidized in the body. For this calculation the amounts of alcohol in the exhaled air and the urine were determined. No examination of the feces for alcohol was easily practicable; but as it has been found in other experiments¹ that no alcohol was excreted through this channel even when considerable quantities were ingested, it was here assumed that the feces would contain no appreciable amount of the alcohol taken with the food.

Considerable attention was given to the methods of determining the amounts of alcohol eliminated by the body. The most satisfactory appeared to be the determination of so-called reducing material by means of sulphuric acid and potassium dichromate. This gives a very delicate reaction with alcohol, but is inaccurate in that other kinds of organic matter have a similar reducing action. To find the amount of such organic matter tests were made in six of the experiments without alcohol, Nos. 26, 28, 29, 31, 32, and 34. The quantities of reducing material eliminated per day, reckoned as alcohol, were: in urine .01-.03 grams, averaging .02 g.; in respiratory products, .24-.36 g., averaging .30 g.; total, .26-.38 g., averaging .32 g. The total reducing material in the 13 alcohol experiments was: in urine .05-.53; in respiratory products, .98-2.76; total, 1.05-2.98 g.; the average total being 1.6 grams per day. Deducting from the .3 g. of material not alcohol, the actual amounts of alcohol excreted per day ranged from .7 to 2.7 grams per day, and averaged 1.3 grams, while the amount taken averaged 72.3 grams daily in the 13 experiments. Accordingly the alcohol given off from the body ranged from 1.0 to 3.7 per cent., and averaged 1.9 per cent. of that ingested, which implies that 98.1 per cent. was oxidized. But our experience implied that the figures for alcohol excreted were really too large; it seems fair to infer, therefore, that certainly not less and probably more than 98 per cent. of the alcohol was burned in the body.²

Accordingly 98 per cent. is taken as the coefficient of availability of alcohol in these experiments.

So far as I am aware, no one else has taken the pains to test the

¹ See Bodländer in *Arch. Physiol.*, Pflüger, xxxii. (1883), p. 424.

² See Benedict and Norris on "The Determination of Small Quantities of Alcohol," *Jour. Am. Chem. Soc.* xx. (1898) p. 299. Compare, also, Dupré, *Proc. Roy. Soc. (London)* xx. (1871-72) 268. See, also, Billings, Mitchell, and Bergey on "The Composition of Expired Air and its Effect upon Animal Life," *Smithsonian Contributions to Knowledge*, xxix. (1895), No. 989.

amounts of alcohol and other organic matters excreted during long periods in experiments with men. The experiments on the subject summarized in the previous chapter (pages 178-181) seem to us to accord with the view that with the precautions observed in our experiments the results would have been similar. We have ventured to assume that our results represent a near approach to the actual proportions of alcohol which escaped oxidation in our own experiments, and that these experiments are probably a fair index of the oxidation of alcohol generally when taken in moderate quantities and ordinary conditions.

Conclusion. — The conclusion is that in the average of these experiments at least 98 per cent. of the alcohol taken was actually oxidized in the body. Other experiments¹ show that in ordinary diet about 98 per cent. of the carbohydrates, 95 per cent. of the fats, and 93 per cent. of the protein are burned in the body. Accordingly the alcohol was more completely oxidized than are the nutrients of ordinary mixed diet.

In these experiments the results with three different men were practically the same. The most reliable investigations elsewhere have given more or less similar figures. The natural inference is that when alcohol is taken in moderate quantities and under ordinary circumstances it is burned even more completely than are the nutrients of ordinary food.

Metabolism of the energy of alcohol.

It was stated above that the experiments with men in the respiration calorimeter had shown a very close agreement between the income and outgo of energy in the body, and that this was regarded as practically a demonstration that the law of the conservation of energy holds in the living organism. Up to April, 1900, the results of thirty such experiments had been obtained. These covered, all told, ninety-three days; they were made with four different subjects, under various conditions of diet and occupation. When the figures for individual days or for individual experiments are considered, there appears to be more or less disagreement between the figures for income and those of outgo of energy, though the differences are inside the natural range of error in such physiological experiments. When the results of all the experiments are averaged together, however, the differences counter-balance each other, and the daily income, 2718 calories, is found to be practically identical with the daily outgo, 2723 calories.² This agreement is in accordance with the law of the conservation of energy, and

¹ Compare Table 2, page 242.

² Later experiments confirm these results.

thus confirms the belief that this law governs the metabolism of energy in the living organism.

In thirteen of the thirty experiments referred to alcohol formed a part of the diet. The results of these experiments compared with those without alcohol imply very clearly that the law of the conservation of energy holds as well with the diet containing alcohol as with the ordinary diet. This may be seen in Table 3, which epitomizes the more detailed statistics and compares the averages of the results of the rest and the work experiments in which alcohol formed a part of the diet with those of similar experiments without alcohol.

TABLE 3.—*Metabolism of energy. Averages of results of experiments with ordinary and with alcohol diet.*

Experiments with and without alcohol.	Energy of income.	Energy of outgo measured as		
		Heat.	Muscular work.	Total.
MORE DIRECTLY COMPARABLE.	Calories.	Cal.	Cal.	Cal.
<i>Rest experiments.</i>				
Without alcohol: Nos. 9, 24, 26, and 28	2185	2221	—	2221
With alcohol: Nos. 10, 22, 27	2186	2221	—	2221
<i>Work experiments.</i>				
Without alcohol: Nos. 11, 29 and 31, 32 and 34	3668	3451	220	3671
With alcohol: Nos. 12, 30, 33	3698	3461	215	3676
<i>Average of rest and work experiments.</i>				
Without alcohol	2927	2836	(110) ¹	2946
With alcohol	2942	2841	(108) ¹	2949
LESS DIRECTLY COMPARABLE.				
<i>Rest experiments.</i>				
Without alcohol: Nos. 13 and 14, 5, 21 .	2301	2277	—	2277
With alcohol: Nos. 7, 15 to 17, 18 to 20	2356	2358	—	2358
<i>Average of all above experiments.</i>				
Without alcohol	2718	2650	(73) ¹	2723
With alcohol	2747	2680	(72) ¹	2752

¹ In these averages the muscular work of the work experiments is distributed over both the work and the rest experiments, which is of course not strictly logical.

The energy of income given in the table above represents the potential energy of the material actually oxidized in the body, the amount of that material being found by subtracting the unoxidized residues of the excretory products from the total food, the body material stored or lost being duly taken into account. The energy of outgo is that given off from the body in the forms of heat and external muscular work,

and measured by the respiration calorimeter. According to the law of the conservation of energy, the income and the outgo must be equal. From the comparisons given in the table above it will be seen that whether the diet did or did not contain alcohol, the outgo was sometimes greater and sometimes less than the income, but the difference in every case was far within the range of variation to be expected in physiological experiments of this nature, so that the results may be considered as showing practical agreement. If we counterbalance the variations by averaging the experiments in which alcohol formed part of the diet and those without alcohol, we have the following figures : —

	Daily income and outgo of energy with and without alcohol.	
	Energy of material oxidized in the body.	Energy given off by the body.
	Calories.	Calories.
Average thirteen experiments without alcohol	2718	2723
Average thirteen experiments with alcohol	2746	2752

When the diet contained no alcohol, the energy of the proteids, fats, and carbohydrates burned in the body averaged 2718 calories per day, and was thus practically identical with the energy which was given off by the body as heat or heat and (the heat equivalent of) external muscular work, and averaged 2723 calories per day. When alcohol formed part of the diet the total energy of the proteids, fats, and carbohydrates burned in the body, added to the energy of the alcohol, averaged 2747 calories per day, and the energy given off as heat or heat and external muscular work averaged 2752 calories per day. The total kinetic energy of outgo is equal to the total potential energy of income, whether it be with ordinary diet alone or with ordinary food and alcohol.

For these results there can be but one interpretation. The energy which was latent or potential in the alcohol was wholly transformed in the body, was actually given off from the body, and was exactly recovered as heat or heat and muscular work. Otherwise, how did the body dispose of the energy of the alcohol, and from what other source did it get an exactly equal amount to replace it?

The conclusions, therefore, are : —

1. The law of the conservation of energy obtained with the alcohol diet as with the ordinary diet.

2. The potential energy of the alcohol oxidized in the body was transformed completely into kinetic energy and appeared either as heat or as muscular work or both. To this extent, at any rate, it was used like the energy of the protein, fats, and carbohydrates of the food.

The protection of body material by alcohol.

General considerations. Previous experiments and their explanation. — The belief was formerly quite general that alcohol has a specific pharmacodynamic action in retarding the metabolism of body material, both fat and proteid. As much of the earlier experimenting implied that alcohol in moderate quantities tends to “prevent waste” or “conserve the tissues,” and its oxidation in the body was not understood, this effect was naturally attributed to its action as a drug. Later, as the functions of the non-nitrogenous nutrients of food came to be better understood, and the fact that alcohol is oxidized as they are in the body became fully established, the view has become common that its effect in retarding or protecting metabolism is to be explained by its action as food rather than as a drug — that, in other words, it tends, by its own oxidation, to prevent the oxidation of other materials. This latter function of alcohol, however, has been denied on two grounds: —

1. The increased circulation of the blood through the peripheral capillaries and the fall of body temperature which follows the ingestion of alcohol have led to the theoretical inference that the energy supplied to the body by the oxidation of the alcohol is lost by the extra radiation of heat it causes, so that it cannot do the work of the fats and carbohydrates in protecting food or body material from consumption. This ground, however, is hardly tenable, since, as shown beyond, the fall of body temperature with ordinary doses is very small, and the amount of extra heat radiated is only a fraction of that supplied by the alcohol.

2. The other ground for doubting the power of alcohol to protect body material from consumption is that of direct experiment. That it may protect fat is generally conceded, but there are a number of reliable experiments on record in which the replacement of the carbohydrates and fats of a ration by alcohol has been followed by an increased elimination of nitrogen. This has been explained by the assumption that alcohol tends to increase rather than diminish the katabolism of protein in the body. On the other hand, there is a considerable amount of experimental evidence to the effect that alcohol may and at times does serve as a protector of protein.

As explained in a review of the experimenting upon this subject in the previous chapter, the conflicting results may be explained by the

hypothesis of two opposing tendencies of alcohol, the one pharmacodynamic and the other nutritive. This view makes the former a specific, and sometimes, if not always, temporary action of alcohol, by which it increases the katabolism of protein, while the latter action is that resulting from its oxidation. According as the latter or the former action predominates the alcohol may protect protein or fail to do so. In favor of this theory is the fact that it explains and harmonizes the results of previous experimenting as it does those of our own experiments also.

In considering the efficiency of alcohol for the protection of body fat and protein it is important to distinguish between two questions. Does alcohol protect these materials at all? Is it equal in protecting power to the isodynamic amount of fats or of carbohydrates, or of a mixture of the two? The comparisons in these experiments are between nearly isodynamic amounts of alcohol and the other ingredients.

The evidence of the experiments here reported.—Although the present experiments were not planned for the study of these particular questions, they throw some light upon them. The details, in their bearing upon the protection or non-protection of body protein and fat are brought together in Table 4 herewith, which shows the amounts of available protein and energy of the diet and the amounts of protein and fat gained or lost by the body in the experiments with and without alcohol:—

TABLE 4. — *Material and energy supplied and metabolized in experiments with and without alcohol.*

[Quantities per day.]

Classification, serial numbers, and subject of experiments.	In food.		Gain (+) or loss (—) of body material.		Energy of mate- rial oxidized in the body.	Energy measured as —		
	Available protein.	Available energy.	Protein.	Fat.		Heat.	Mus- cular work.	Total.

<i>Class I. — Experiments with and without alcohol more strictly comparable.</i>								
REST EXPERIMENTS.								
GROUP A.								
No. 9, E. O., ordinary diet.....	112	2426	— 3.6	+18.3	2274	2309	2309
No. 10, E. O., alcohol diet.....	115	2427	— 6.7	+21.0	2265	2283	2263
GROUP B.								
No. 24, E. O., ordinary diet.....	115	2809	+ 1.7	+60.1	2227	2272	2272
No. 22, E. O., alcohol diet.....	117	2777	+ 1.2	+63.1	2168	2259	2259
GROUPS A AND B.								
Average 9, 24, E. O., ordinary diet	114	2618	— 1.0	+39.2	2251	2291	2291
Average 10, 22, E. O., alcohol diet	116	2602	— 2.8	+42.1	2217	2271	2271

TABLE 4. — *Continued.*

Classification, serial numbers, and subject of experiments.	In food.		Gain (+) or loss (—) of body material.		Energy of mate- rial oxidized in the body.	Energy measured as —		
	Available protein.	Available energy.	Protein.	Fat.		Heat.	Mus- cular work.	Total
Class I. — Continued.								
GROUP C.								
No. 26, J. F. S., ordinary diet	93	2256	—3.3	+24.2	2043	2085	2085
No. 28, J. F. S., ordinary diet	91	2249	—4.6	+21.9	2066	2079	2079
Average 26, 28.....	92	2253	—4.0	+23.1	2055	2082	2082
No. 27, J. F. S., alcohol diet.....	92	2264	—6.0	+18.1	2125	2123	2123
GROUPS A, B, AND C.								
Average 9, 24, 26 + 28, ordinary diet	106	2496	—2.0	+33.8	2185	2221	2221
Average 10, 22, 27, alcohol diet ...	108	2489	—3.8	+34.1	2186	2221	2221
WORK EXPERIMENTS.								
GROUP D.								
No. 11, E. O., ordinary diet.....	110	3510	—3.0	—40.1	3909	3745	186	3931
No. 12, E. O., alcohol diet	113	3614	—1.0	—32.5	3928	3727	200	3927
GROUP E.								
No. 29, J. F. S., ordinary diet.....	95	3260	—5.0	—23.9	3517	3334	255	3589
No. 31, J. F. S., ordinary diet	96	3275	—2.3	—16.0	3441	3171	249	3420
Average 29, 31	96	3268	—3.7	—20.0	3479	3253	252	3505
No. 30, J. F. S., alcohol diet.....	95	3242	—13.1	—17.2	3480	3321	249	3470
GROUP F.								
No. 32, J. F. S., ordinary diet.....	93	3226	—5.0	—35.1	3500	3369	196	3565
No. 34, J. F. S., ordinary diet.....	92	3241	—11.4	—35.5	3644	3337	250	3587
Average 32, 34	93	3234	—8.2	—35.3	3617	3353	223	3576
No. 33, J. F. S., alcohol diet	92	3227	—15.4	—38.9	3685	3435	197	3632
GROUPS E AND F.								
Average 29 + 31, 32 + 34, ordinary diet	95	3251	—6.0	—27.6	3548	3303	238	3541
Average 30, 33, alcohol diet.....	94	3235	—14.3	—28.1	3583	3328	223	3551
GROUPS D, E, AND F.								
Average 11, 29 + 31, 32 + 34, ordi- nary diet	100	3337	—5.0	—31.8	3668	3451	220	3671
Average 12, 30, 33, alcohol diet	100	3361	—9.8	—29.5	3698	3461	215	3676
GROUPS A TO F.								
Average 9, 24, 26 + 28, 11, 29 + 31, 32 + 34, ordinary diet	103	2917	—3.5	+1.0	2927	2836	110	2946
Average 10, 22, 27, 12, 30, 33, alco- hol diet.....	104	2925	—6.8	+2.3	2942	2841	108	2949
Class II. — Experiments with and without alcohol less strictly com- parable.								
REST EXPERIMENTS.								
GROUP G.								
No. 13, E. O., ordinary diet.....	110	2298	—11.7	+27.1	2106	2151	2151
No. 14, E. O., ordinary diet.....	89	2289	—12.2	+24.5	2124	2193	2193
Average 13, 14.....	100	2294	—12.0	+25.8	2115	2172	2172
No. 7, E. O., alcohol diet.....	99	2230	—12.0	—14.4	2437	2394	2394
GROUP H.								
No. 5, E. O., ordinary diet.....	109	2384	—4.2	—7.8	2482	2379	2379
No. 15, E. O., alcohol diet	104	2426	+5.6	+3.9	2358	2362	2362
No. 16, E. O., alcohol diet	104	2424	+6.9	+5.3	2335	2332	2332
No. 17, E. O., alcohol diet	104	2427	+5.8	+11.0	2288	2276	2276
Average 15, 16, 17.....	104	2426	+6.2	+6.7	2327	2324	2324
GROUP I.								
No. 21, A. W. S., ordinary diet.....	90	2038	—5.4	—25.2	2308	2279	2279
No. 18, A. W. S., alcohol diet.....	90	2532	—11.9	+25.6	2362	2488	2488
No. 19, A. W. S., alcohol diet	90	2550	+3	+35.8	2214	2279	2279
No. 20, A. W. S., alcohol diet	90	2549	+2.2	+21.9	2335	2303	2303
Average 18, 19, 20	90	2544	—3.1	+27.7	2303	2357	2357

TABLE 4. — *Continued.*

Classification, serial numbers, and subject of experiments.	In food.		Gain (+) or loss (—) of body material.		Energy of mate- rial oxidized in the body.	Energy measured as —		
	Available protein.	Available energy.	Protein.	Fat.		Heat.	Mus- cular work.	Total.

<i>Class II. — Continued.</i>								
GROUPS G, H, AND I.	Gr.	Cal.	Gr.	Gr.	Cal.	Cal.	Cal.	Cal.
Average 13 + 14, 5, 21, ordinary diet	100	2239	— 7.2	— 2.4	2301	2277	2277
Average 7, 15 to 17, 18 to 20, alcohol diet.....	98	2400	— 3.0	+ 6.8	2356	2358	2358
<i>Class III. (including I. and II. to- gether).</i>								
GROUPS A TO I.								
Average 9, 24, 26 + 28, 11, 29 + 31 32 + 34, 13 + 14, 5, 21, ordinary diet	102	2691	— 4.7	— .1	2718	2650	73	2723
Average 10, 22, 27, 12, 30, 33, 7, 15 to 17, 18 to 20, alcohol diet	102	2750	— 5.5	+ 3.8	2747	2680	72	2752

When the fuel value of the diet is in excess of the needs of the body, the latter may and often does increase its store of material. Sometimes this increase is in the form of protein, sometimes fat, and sometimes both protein and fat. When the body requires energy in excess of that supplied by the food, it will draw upon its previously accumulated store of fat or protein, or both, for fuel. Along with the gains and losses of protein and fat are changes in the carbohydrates (glycogen), but the total quantity of these substances in the tissues is relatively small. The present methods of experimenting do not suffice for accurate measurement of the changes of glycogen, and it is commonly left out of account in discussions such as that in which we are now engaged.

Protection of body fat.

The figures for the individual experiments in Table 4 show in some cases a larger gain or smaller loss of fat without alcohol than with it; in other cases the results are reversed. When, however, the experiments are grouped together and the averages with and without alcohol are compared, it is clear that, except where the differences in fuel value of the diet were considerable, the differences of fat balance are hardly large enough to be of consequence. Taking the experiments altogether, the figures show slight gains in fat both with and without alcohol, but the gain is slightly larger with the alcohol. The comparison shows, on the whole, an advantage of the ordinary diet over that with alcohol, though the difference is very small, indeed.

A direct indication of the fat-protecting power of alcohol is found

in the series of experiments with E. O., Nos. 22, 23, 24.¹ These were practically three successive periods of 3 days each. In all there was a basal ration with 116 grams available protein and 2290 calories of available energy. To this ration was added—in the first experiment, alcohol; in the second, nothing; in the third, sugar. The alcohol and sugar each furnished about 500 calories of energy. With the alcohol there was a daily gain of 63 grams of fat; with the basal ration this was reduced to 9 grams; with the sugar it rose again to 60 grams per day. With the sugar there was a gain of 1.7 and with the alcohol a gain of 1.2 grams of protein, while with the basal ration alone there was a loss of 1.7 grams of protein. Taking this slight gain or loss of protein into account, the net gain of fat with the alcohol above that in the basal ration was 54 grams, which would make very nearly 500 calories. The net gain of fat with sugar was 51 grams. In this particular case, therefore, with isodynamic quantities of sugar and alcohol, the gain of fat was practically the same with both.

An even more striking illustration of the fat-protecting power of alcohol is found in experiments Nos. 18–21, with A. W. S.¹ When alcohol was added to a basal ration of ordinary food, in Nos. 18–20, the body gained fat at the rate of 21–35 grams per day; but when the giving of alcohol was stopped and the body had only the basal ration in No. 21, it lost 25 grams of fat per day.

A clearer demonstration of the power of alcohol to protect fat from consumption would be hardly possible than that given in the experiments with E. O. and A. W. S., just cited. The basal ration to which the alcohol was added was, with E. O., sufficient, and with A. W. S., insufficient to maintain the store of fat in the body. We thus have two kinds of tests of the power of alcohol as compared with that of isodynamic amounts of carbohydrates and fats of the food for the protection of body fat. In every individual case the protecting power of the alcohol is manifest. In some instances it is slightly inferior, and in others it is slightly superior in this respect, and on the average it is just about equal to the nutrients which it replaced.

The conclusion is that in these experiments the fat protection in the alcohol rations was very slightly different from that with the ordinary rations, in other words the alcohol was practically as efficient in the protection of body fat as the fats and carbohydrates of the food which it replaced.

So far as I am aware these are the only experiments in which the power of alcohol to protect fats has been determined by direct quantitative tests. While there are numerous experiments on record which have seemed to indicate that alcohol has this power, I have found

¹ See the Memoir above referred to for details.

none which seem to imply the opposite.¹ Fortunately this question, which is one of no little importance, thus seems to be so clearly settled as to require no further discussion. Such is not the case with the similar question regarding the power of alcohol to protect protein from consumption.

Protection of body protein.

As regards the protection of body protein by alcohol, the results of the experiments are variable, but on the whole the katabolism of protein, as measured by the amount of nitrogen excreted by the kidneys, was slightly larger in the experiments with alcohol than in those without.

As the practical bearings of the subject are discussed in the chapter which follows, the results of other experimenting are summarized in the preceding chapter, and the details of our own experiments are given in the Memoir above cited (page 239), it will suffice to give the main facts and final conclusions.

What especially concerns us here is the influence of the substitution of alcohol for a portion of the ordinary food upon the gain or loss of body protein. As this seems to depend largely upon the individual, it will be well to discuss the experiments with the three subjects separately.

One thing has impressed us, not only in these experiments but in others, the results of which we have studied. It is that the daily nitrogen balance is a much less reliable indication of the effects of diet, or of drugs, or of muscular work, or of medical treatment than is commonly supposed.²

Experiments with E. O. — With this subject there was a marked tendency to excrete more nitrogen in the urine on either the day before or the day after he entered the respiration chamber. This tendency was as noticeable in the experiments without as in those with alcohol. This variation in nitrogen excretion is independent of either the character of the food or the activity of the subject, and appears to be due to a psychic cause that is little understood. Since this variation was often much larger than any which could be attributed to the alcohol, we hesitate to assign to the latter any definite and uniform effect upon the metabolism of nitrogen.

It is to be noted that there is no experiment with E. O. in which an alcohol diet immediately preceded or followed a diet furnishing the same amount of energy from ordinary food materials without alcohol.

¹ See references to experiments on the influence of alcohol upon the metabolism of carbon compounds in the previous chapter.

² See discussion of this on page 209.

There are, however, a number of separate experiments which may be compared, as is done in Table 5.

TABLE 5.—*Experiments with E. O. Gains and losses of body protein and fat with and without alcohol.*

Experiments.	Total number of days.	Average per day.			
		In available food.		Gain (+) or loss (—).	
		Protein.	Energy.	Protein.	Fat.
MORE DIRECTLY COMPARABLE.					
<i>Rest experiments.</i>					
Without alcohol, Nos. 9, 24 . .	7	114	2618	— 1.0	+ 39.2
With alcohol, Nos. 10, 22 . .	7	116	2602	— 2.8	+ 42.1
<i>Work experiments.</i>					
Without alcohol, No. 11 . . .	4	110	3510	— 3.0	— 40.1
With alcohol, No. 12	4	113	3614	— 1.0	— 32.5
<i>Rest and work experiments.</i>					
Without alcohol, Nos. 9, 24, 11	11	112	2915	— 1.6	+ 12.8
With alcohol, Nos. 10, 22, 12 .	11	115	2939	— 2.2	+ 17.2
LESS DIRECTLY COMPARABLE.					
<i>Rest experiments.</i>					
Without alcohol, Nos. 13, 14, ¹ .	7	99	2294	— 12.0	+ 25.8
With alcohol, No. 7	4	99	2230	— 12.0	— 14.4
AVERAGE OF ALL ABOVE.					
Without alcohol	18	109	2760	— 4.2	+ 16.0
With alcohol	15	111	2762	— 4.6	+ 9.3

¹ Nos. 13 and 14 averaged as one experiment.

In the less directly comparable experiments Nos. 13 and 14 are grouped together as one, since the average quantities of protein and energy are the same as in No. 7. The details, however, show that while the quantities of energy in the rations were the same in both, No. 13 had 110 and No. 14 only 89 grams of protein. Nevertheless the results as regards gain or loss of body material were almost identical. In each there was a loss of 12 grams of protein, and in No. 13 there was a gain of 27 grams, and in No. 14 a gain of 24 grams of fat. The experiments were 40 days apart. We lay especial stress upon this circumstance, because it illustrates the futility of drawing final conclusions from a single experiment. In each of these cases the metabolism experiment was preceded by a period of 4 days with similar diet while the subject was outside the calorimeter, but in neither case was nitrogen equilibrium obtained. Neither one of these experiments, therefore, could be taken as a basis for conclusion as to the quantity of protein required for either nitrogen equilibrium or con-

stant elimination of nitrogen. A special reason for citing them here with No. 7 is that they were made with the same subject as the other experiments of the table.

The chief reliance is to be placed upon the more directly comparable experiments. In those in which the subject was at rest, the alcohol ration furnished 2 grams more protein and 16 less calories of energy per day than the non-alcohol ration. There was a larger loss of protein by 1.8 grams and a larger gain of fat by 3 grams with the alcohol. These differences are all very small, but in so far as they go they imply that the alcohol was somewhat less efficient as a protector of protein than the fats and carbohydrates which it replaced. In the work experiments the alcohol ration supplied 3 grams more of protein and 104 calories more of energy than the other. With both there was a loss of protein, the amount being 3 grams per day without and 1 gram per day with alcohol; but since the alcohol ration furnished 3 grams of protein more than the other, there remains a deficit of 1 gram of protein per day against the alcohol ration as compared with that without alcohol, and that notwithstanding the larger fuel value of the diet. Here again the alcohol ration is slightly inferior in protein protecting power.

Taking the rest and work experiments together, the alcohol rations, with an average of 3 grams of protein and 24 calories of energy per day more than the non-alcohol ration, show a greater loss of protein by 0.6 gram per day. On the other hand, there is a slightly larger average gain of fat with the alcohol.

If we reckon the less comparable experiments in the general average, we have 111 grams of protein with alcohol as against 109 grams without it, while the quantities of energy are the same in both rations. The average loss of protein is 0.4 gram greater and the gain of fat 5.6 grams less with the alcohol; but of course much less stress is to be laid upon the less comparable experiments.

On the whole it is clear that in these experiments with this subject the alcohol was not as efficient as isodynamic quantities of fats and carbohydrates in protecting protein.¹ Notwithstanding the energy of the alcohol was actually larger than that of the fats and carbohydrates which it replaced, it did not equal them in protecting power. The

¹ Rosemann interprets two of our experiments, Nos. 7 and 10, the only ones then published, as not showing the protection of protein; an interpretation from which we should not dissent, since No. 7 was exceptional, and two experiments could hardly suffice for the establishment of the principle. Rosenfeld, on the other hand, interprets the same experiments as indicating that the alcohol protected both fat and protein, and that it "plays the same rôle as fats and carbohydrates in metabolism."

difference is the more striking because of the slightly larger average quantities of protein in the alcohol rations. On the other hand, the differences between the amounts of protein and energy in the alcohol as compared with the non-alcohol experiments are so slight as to imply only a slight inferiority of the alcohol in the protection of protein.

While the alcohol was not isodynamically equal to the carbohydrates and fats in protecting power, it would be going very far to deny that the experiments imply a positive protecting action. Not only were the differences in favor of the protecting power of the carbohydrates and fats as compared with the alcohol very small, but the quantity of energy supplied by the alcohol was large. To claim that the alcohol has no protecting power would be to assume that the same reduction of fats and carbohydrates in the rations without any replacement by alcohol would have resulted in no greater differences in protein protection. This is in the highest degree improbable.

In this connection the results of experiments Nos. 22, 23, 24, above referred to, are worthy of consideration. With the normal ration, plus alcohol, there was a gain of 1.4 grams of protein and 63 grams of fat per day; but when, in the period immediately following, the alcohol was removed, there was a loss of 1.6 grams of protein and a gain of only 9 grams of fat.

Experiments with A. W. S. — With this subject we have but one series of rest experiments. This consisted of a preliminary period of 4 days, followed by four experimental periods, during which the subject was in the respiration chamber. Throughout the preliminary and experimental periods there was a uniform basal ration of ordinary food, supplying about 90 grams of protein and 2040 calories of energy. To this was added, in the preliminary period of 4 days, commercial alcohol, furnishing about 500 calories of energy. The nitrogen in the urine during the successive days was 12.2, 16, 19, 16.4 grams; that is to say, there was a marked increase of protein katabolism during the whole period. The first three experiments proper were of 2 days each. In the first of these periods commercial alcohol, in the second whiskey, and in the third brandy was added to the basal rations, the quantities being sufficient to furnish the same amount, about 500 calories, of energy. The daily quantities of nitrogen in the urine were 17.4, 15.4, 14.7, 14.2, 13.8, and 14.4 grams; that is to say, the rise in nitrogen excretion continued through the first day of the first period; thereafter it fell. During the fourth period of 3 days the basal ration was given without the alcohol. The nitrogen excretion was 14.5, 16.2, 15.4 grams, thus showing an increase again. The natural inference is that with this subject, who had always been an abstainer, the rise in nitrogen excretion at first was due to the alcohol. The very evident

fall after the fifth day implies that the action of alcohol in increasing the nitrogen was transitory, and that it had passed away at the end of the third period. The increase of nitrogen excretion in the fourth period was apparently due to the reduction of the ration by the removal of the alcohol.

The average gains and losses of protein and fat for the separate periods may be tabulated as follows:—

Period.	Days.	Alcohol added to basal ration.	Gain (+) or loss (—) grams per day.	
			Protein.	Fat.
First	2	Commercial alcohol . . .	— 12	+ 26
Second	2	Whiskey	+ 1	+ 36
Third	2	Brandy	+ 2	+ 22
Fourth	3	None	— 3	— 25

We thus have a gradual change from a loss of nitrogen to equilibrium and positive gain with the alcohol, and on its removal a positive loss. With the fat there is a constant gain with the alcohol and marked loss on its removal.

While it would be unwise to generalize from a single series of experiments, the indications here point clearly toward three conclusions: (1) The alcohol at first caused an increase of nitrogen metabolism and loss of body protein, but this effect was temporary; (2) thereafter the alcohol protected body protein; (3) the alcohol protected fat throughout.

Experiments with J. F. S.—With the third subject there was opportunity to observe the immediate effect produced upon nitrogen metabolism by the substitution of alcohol for a part of the ordinary nutrients of the diet. Three series of experiments were made. Each included three periods of three days each. In each series the subject received the same basal ration throughout, but in addition thereto enough of either butter, sugar, or alcohol to furnish about 500 calories. In the first series the subject was at rest, and the order of addition was butter, alcohol, sugar. In the second series the subject was at work and received a larger diet, the order being sugar, alcohol, butter. The third series was similar in all respects to the second except that the order was butter, alcohol, sugar.

These experiments were thus better adapted than any of those previously discussed to show the immediate effect of the substitution of alcohol for other nutrients in the diet, and in each case it will be seen that this substitution resulted in a loss (or an increased loss) of body protein, which loss continued through the three days of the alcohol period. The subject was unused to alcoholic beverages, and from

what has already been said such a loss of protein during the first few days of the alcohol diet was to be expected. Whether this loss would have ceased on continuing the alcohol diet, as seems to have been the case with A. W. S., the experiments do not show.

Referring to the figures of Table 4, all of the experiments with this subject would indicate clearly that for periods of three days the alcohol was inferior to either fat or carbohydrates as a protector of protein. It should be stated, also, that the loss of body protein with the alcohol was greater than the figures in the table would indicate, for the nitrogen elimination of the period preceding the alcohol was in each case slightly increased by the entrance of the subject into the respiration chamber, while that of the period following the alcohol is increased by the lag in the excretion of the extra nitrogen metabolized under the influence of the alcohol. The lag would, of course, likewise prevent the effect of the alcohol from becoming fully apparent in the first day of the alcohol period. Hence a better idea of the actual effect of the alcohol would probably be obtained by omitting from consideration the first day of each period. The average elimination of nitrogen thus becomes, in the fore periods, 15.5 grams, in the alcohol periods, 17.1 grams, and in the after period, 15.5 grams per day, showing a difference in favor of the ordinary nutrients of 1.6 grams of nitrogen, or 10 grams of protein instead of 6.2 grams as shown in the preceding table.

It is also noticeable that the loss of body protein under the influence of alcohol was larger with this subject when at work than when at rest. The difference is not great and may be simply accidental. It might, however, be interpreted as indicating that the subject worked to better advantage on the ordinary diet than on the diet of which a part was alcohol. This would accord with the conclusions drawn by Chauveau from experiments on dogs¹ and by Parkes from extended observations on marching soldiers and workingmen.²

Summary. — In interpreting these experiments two things are to be considered. One is that the differences between the amounts of nitrogen excreted with and without alcohol are generally very small. The other is that there is good ground for the belief that with persons little accustomed to the use of alcohol it may have a tendency to increase nitrogen metabolism, which may counteract, to a greater or less extent, the tendency to protect protein, though, with some persons at least, this action appears to be temporary. The results with the individual subjects may be briefly recapitulated as follows: —

¹ *Compt. rend. Acad. des Sc.* par. 132, pp. 65 and 110.

² *Proc. Roy. Soc.* xx. (1871-72), 402, and monograph, "On the issue of a spirit ration during the Ashantee campaign, 1874," etc., London, 1875.

With E. O., who was accustomed to the use of moderate quantities of alcoholic beverages, the protein protecting power of the alcohol was apparent, but seemed to be somewhat inferior to that of fats and carbohydrates.

With A. W. S., an abstainer, there was an increase of nitrogen excretion during the first days after the beginning of the alcohol diet, with a resulting loss of body protein, but this action ceased after five or six days, and thereafter the alcohol apparently protected protein, though the experiments do not show how its efficiency in this respect compared with that of the carbohydrates and fats.

With J. F. S., who was also an abstainer, there was, in each case, an increase of nitrogen excretion and loss of body protein during the three-day periods in which the alcohol replaced fat or sugar. There was thus a marked inferiority of alcohol in protecting power. The result is similar to that observed with A. W. S. during the first days with alcohol, but the experiments do not show what the effect of continuing the alcohol diet would have been, and they are, therefore, not decisive.

Taking the results of all the experiments together, it may be said that —

1. They offer no evidence to imply that alcohol cannot protect protein, though they imply in some cases it may, at least for a time, fail to do so.
2. On the other hand, they give very marked indications of its protein protecting power.
3. They imply clearly that in this respect it was in some cases nearly or quite equal and in others decidedly inferior to the isodynamic amounts of carbohydrates and fats which it replaced.

It is clear that the experiments above described are not conclusive regarding the action of alcohol in protecting protein from consumption. They were not planned for the study of this subject. To make the results decisive the alcohol periods should be long enough to eliminate the more or less temporary action of alcohol as a drug; the available energy of the ration of the non-alcohol periods should equal in some cases the total available energy of the alcohol ration, while in other cases it should equal only that of the ordinary food of the alcohol ration, and finally, the experiments should be repeated with different persons and under different conditions. These facts we did not fully understand when the experiments were begun, nor would it have been practicable with the means at our disposal to make such experiments with men in the respiration calorimeter as would be needed for the comprehensive study of the question. Experiments of from twenty to thirty consecutive days seem necessary for the most satisfactory results.

For a man to spend so long a time in the respiration chamber of our apparatus would be, to say the least, very tedious, and the cost of such experiments, in labor and money, would have exceeded our available resources. Fortunately, the results obtained by a number of other investigators, while our experiments were being made and since, have done much to clarify the situation as regards the effects of alcohol upon protein metabolism, as explained in the previous chapter.

Final conclusions regarding the influence of alcohol upon protein metabolism.—The experiments and considerations above cited seem to us to warrant the following conclusions:—

1. The power of alcohol to protect the protein of food or body tissue, or both, from consumption is clearly demonstrated. Its action in this respect appears to be similar to that of the carbohydrates and fats; that is to say, in its oxidation it yields energy needed by the body, and thus saves other substances from oxidation. In this way alcohol serves the body as food. Just how moderate quantities of alcohol compare with isodynamic amounts of sugar, starch, and fat in the power to protect protein from katabolism is not yet settled. Apparently it is in some cases equal, in others inferior, to these substances. It is by no means certain that the fats and carbohydrates are always equal to each other in this power.

2. Alcohol appears also to exert at times a special action as a drug. In large quantities it is positively toxic, and may retard or even prevent metabolism in general and proteid metabolism in particular. In small doses it seems at times to have an opposite influence, tending to increase the disintegration of protein. This action, though not conclusively demonstrated, is very probable. It offers a satisfactory explanation for the occasional failure of alcohol to protect protein, the assumption being that the two tendencies counteract each other. The only justification for calling alcohol a proteid poison is found in this disintegrating tendency. This pharmacodynamic action of alcohol appears to be temporary and most apt to occur with people little accustomed to its use. The circumstances under which such action occurs cannot now be fully defined.

Influence of coffee upon protein metabolism in these experiments.

In some of these experiments alcohol was administered with coffee, in others with water. It might be thought that the presence of the coffee would interfere with the action of the alcohol.¹ The figures give no support for this view, as is shown in the following tabular statement:—

¹ See Woodbury and Egbert, "A Physiologic Consideration of the Food Value of Alcohol," *Jour. Am. Med. Asso.*, March 31, 1900.

Elimination of nitrogen in presence and absence of coffee.

[Quantities per day.]

Kind and number of experiments.	Days.	Nitrogen.			
		In food.	In feces.	In urine.	Gain (+) or loss (-) to body.
I. With coffee :		Grams.	Grams.	Grams.	Grams.
a Average 4 experiments with alcohol [10, 12, 18, 22].....	13	18.6	1.2	18.2	-0.8
b Average 4 experiments without alcohol [9, 11, 21, 24].....	14	18.6	1.5	17.5	-0.4
c Increase (+) or decrease (-) with alcohol, a-b.....		0	-0.3	+0.7	-0.4
II. Without coffee :					
d Average 5 experiments with alcohol [(19, 20), 27, 30, 33].....	13	15.8	1.0	16.1	-1.3
e Average 7 experiments without alcohol [21, (26, 28), (29, 31), (32, 34)]	21	15.9	1.0	15.7	-0.8
f Increase (+) or decrease (-) with alcohol, d-e.....		-0.1	0	+0.4	-0.5
g Apparent influence of coffee, c-f.....		+0.1	-0.3	+0.3	+0.1
III. Direct comparison, alcohol with and without coffee :					
h Experiments 15, 17, 18, alcohol given with coffee.....	6	16.5	0.9	16.0	-0.4
k Experiments 16, 19, 20, alcohol given without coffee.....	6	16.5	1.0	14.9	+0.6
Apparent influence of coffee, h-k.....		0	-0.1	+1.1	-1.0

This table comprises all of the experiments that are directly comparable. The experiments in which the alcohol was given with coffee are averaged together, and compared with the corresponding non-alcohol experiments, and the figures in the third line of category I. show the effects of alcohol in presence of coffee. Under II. a similar comparison is made of the experiments in which no coffee was given, the third line of figures here showing the effects of alcohol, when taken alone. By subtracting the third line of figures under II. from the corresponding figures under I., we obtain values which may be taken as showing the influence of the coffee. A more direct comparison of results with and without coffee is given under III., but the number of experiments compared is necessarily smaller, and therefore individual variations have relatively much greater weight. While the differences which could be attributed to the coffee are hardly outside the limits of experimental error, it would seem that if there is any effect, it is to increase rather than to retard proteid metabolism.

Effect of alcohol upon the radiation of heat from the body.

A current theory maintains that although alcohol supplies heat to the body, it also increases the radiation of heat from the body, so that much or all the energy it supplies is wasted.

This theory is based upon two kinds of evidence, which are well attested and make it very plausible. One is the distension of the blood vessels which cause the flush of the skin when alcohol is taken. The other is the lowering of the temperature of the body after the ingestion of alcohol, which is shown by many experiments and is explained by the loss of heat.

Some writers even go so far as to claim that the extra heat radiation due to the distension of the peripheral vessels is greater than the heat supply from the oxidation of the alcohol. According to this view, alcohol, instead of being a source of energy, is a cause of its loss to the body.

The difficulty with the theory is the exaggeration of the influence of small quantities of alcohol in increasing heat radiation. While the temperature of the body has been found to fall considerably after the ingestion of large doses of alcohol, and especially under exposure to great cold, the effect of ordinary doses is slight and often imperceptible.

In the experiments here described the determinations of body temperature were made with an ordinary clinical thermometer in the mouth and axilla, as elsewhere stated. This method, which is the one ordinarily followed, does not give results as accurate as are to be desired. In some of the earlier experiments, especially with E. O., the observations are of doubtful value. Steps have been taken in this laboratory to devise a thermometer and method of observation which will show more accurately the variations of internal temperature of the body.¹ Meanwhile, as may be seen from the detailed figures in the memoir, it is clear that the observations do not imply that the bodily temperatures with and without alcohol were greatly different. This agrees with the results of other investigations.²

¹ F. G. Benedict and J. F. Snell, "Eine neue Methode um Körpertemperaturen zu messen," *Archiv. f. d. ges. Physiologie*, lxxxviii. 492 (1901).

² The results of the most reliable observations are well summarized by Pembrey (Schaefer's *Physiology*, i. 820) in the following statements:—

"Various observers have found that alcohol taken in ordinary quantities as a beverage causes a slight depression, generally less than half a degree in the temperature of healthy men. On the other hand, poisonous doses may cause a fall of 5° or 6°—in fact, many of the lowest temperatures recorded in man have been observed in drunk persons exposed to cold. See Davy, *Phil. Trans.*, London, 1850, p. 444; Lichtenfels and Fröhlich, *Denkschriften d. k. Akad. d. Wissensch.*, Wien, 1852, Bd. iii. Abth. 2, S. 131; Lallemand, Perrin, and Duroy, 'Du rôle de l'alcool et des anesthésiques dans l'organisme,' Paris, 1860; Ogle, *St. George's Hosp. Rep.*, London, 1866, vol. i. p. 233; Ringer and Rickards, *Lancet*, London, 1866, vol. ii. p. 208; Cuny Bouvier, *Arch. f. d. ges. Physiol.*, Bonn, 1869, Bd. ii. S. 370; Godfrin,

The alcohol used in these experiments was equivalent to about 72 grams of absolute alcohol per day taken in 6 doses. This is about the amount contained in an ordinary bottle of wine with 10 per cent. alcohol, or 3 or 4 glasses (6 or 8 ounces) of whiskey.

If we use our own observations and the others just referred to as a basis, it would seem that the fall of body temperature produced by such amounts of alcohol might ordinarily range from nothing to one half of a degree centigrade. The heat which the body of an average man would have to lose in order to reduce the temperature one half of a degree might be roughly calculated as follows:—

We may take the weight of the body of the average man at 148 pounds, or 67 kilos. The specific heat of the body is not exactly known, but may be estimated at 0.83. On this base a fall of temperature of one half of a degree centigrade would correspond to 1.2 (67×0.83), or about 28 calories. Of the 72 grams of alcohol, 98 or 99 per cent., or between 70 and 71 grams, would be burned in the body, and would yield at 7.1 calories per gram about 500 calories of heat. By this estimate, if the 72 grams of alcohol were taken in one dose, and caused a lowering of the body temperature by one half of a degree, the 28 calories of heat wasted in the extra radiation due to the alcohol would be one eighteenth the amount supplied by its combustion.

This method of calculating the amount of heat which the body must lose in order to produce a given fall of temperature is hardly correct. It would be so if we had to do only with a fixed amount of heat at the outset and a fixed amount of loss. But, as a matter of fact, the body is constantly gaining heat from the oxidation of material from within, and constantly losing not only by outward radiation, but in other ways, as in the exhalation of air and water vapor in respiration, in the excretions of the kidneys and intestine, and in the evaporation of water from the skin. The actual temperature depends upon the income and outgo of heat. The income depends upon the material oxidized in the body. The outgo is regulated to a greater or less extent by processes which are not fully understood, but in which the nervous system is the important agency.

Experimental inquiries. — Meanwhile we may consider the experimental evidence bearing directly upon the question of the radiation of heat with and without alcohol.

‘De l’alcool, son action physiologique, ses applications thérapeutiques,’ 1869; Weckerling, *Deutsches Arch. f. klin. Med.*, Leipzig, 1877, Bd. xix. S. 317; Zuntz, *Fortschr. d. Med.*, Berlin, 1887; Geppert, *Arch. f. exper. Path. u. Pharmacol.*, Leipzig, Bd. xxii. 36; Parkes and Wollowicz, *Proc. Roy. Soc. London*, 1870, vol. xviii. p. 362, found that alcohol in ordinary quantities had no effect on the temperature of a healthy man.”

In a series of experiments by Reichert with dogs the effect of alcohol on the radiation of heat was tested.¹ The experimental periods were, however, only 5 or 6 hours each, and there was no complete comparison of the effects of different diets. The rate of heat radiation and the change of body temperature were carefully observed. The results implied a probable but at most very small increase of heat radiation as the result of administering alcohol.

The experiments with men in the respiration calorimeter here described give extended data regarding both the consumption of fuel and the radiation of heat. The details are summarized in Table 4. The final outcome is simple and may be illustrated by two cases, Groups A and D. In each there were two experiments, practically alike, save that one was with ordinary diet and the other with a diet in which part of the fats and carbohydrates were replaced by alcohol as above described. In Group A the subject was at rest, *i. e.* doing no external muscular work. The potential energy of the material burned in the body and the amounts of heat given off in calories were practically the same, as is shown by the figures herewith. The differences in the results without and with alcohol are entirely within the limits of ordinary variation:—

Comparison of energy of material metabolized and heat given off per day in rest experiments with and without alcohol.

Diet.	Energy of material burned.	Energy given off by the body as heat.
	Calories.	Calories.
Without alcohol, experiment No. 9	2274	2309
With alcohol, experiment No. 10	2265	2283

If the alcohol had caused increased radiation of heat, more heat would have been given off from the body and more fuel would have been required, and naturally more would have been burned in the alcohol experiment than in the other. Such, however, was not the case.

In the experiments of Group D the man was engaged for eight hours a day in active muscular work, driving a stationary bicycle. The amount of work was such that he burned enough fuel to yield in all 3900 calories, and, as the food did not supply enough, he used up some of his store of body fat. The results of such experimenting imply that when the body has not enough food for its support and is forced to draw upon its reserve capital, it uses the materials economically.

¹ *Therapeutic Gazette*, February, 1890.

The energy given off from the body was in two forms — heat and external work. This work was practically the same in both experiments and is reckoned with the heat in the energy given off.

Comparison of energy of material metabolized and heat given off per day in work experiments with and without alcohol.

Diet.	Energy of material burned.	Energy given off by the body as heat and muscular work.
	Calories.	Calories.
Without alcohol, experiment No. 11	3909	3922
With alcohol, experiment No. 12	3938	3927

Here again there was slightly more fuel burned per day with alcohol than without, though the difference was small, while the amount of heat given off was practically the same in the one case as the other. So far as the disposal of the energy is concerned, the figures imply that alcohol was used as economically as the fat, sugar, and starch which it replaced, and that it caused no increased radiation of heat.

We have, all told, 13 experiments with alcohol, covering 36 days. For purposes of comparison these have been grouped, as already explained (p. 000), with 13 experiments without alcohol, covering 43 days.

The subject in five of these groups, E. O., was a man who had been long accustomed to the moderate use of alcoholic beverages. The subjects in the other four groups, A. W. S. and J. F. S., were two men who had always been total abstainers.

The results are summarized in the table herewith. The first column gives the figures for energy for material actually oxidized. The figures in the second column show the relation between the averages of experiments with alcohol and those without alcohol, the latter being taken as a basis (100 per cent.). The corresponding values for total and proportional energy measured as heat in the two classes of experiments are shown in the last two columns in the table. Thus, in the average of all the experiments without alcohol the energy of the material actually oxidized was 2718 calories. In the average of all the experiments with alcohol it was 2747 calories. The latter was 101.1 per cent. of the former.¹

¹ A difference so small as this is well inside the range of unavoidable error in single experiments. It is only where a large number of such experiments are averaged that differences of one or two parts in one hundred could probably be regarded as significant.

Comparison of energy of material oxidized and heat given off in experiments with and without alcohol.

[Averages per day.]

	Energy of material oxidized.		Heat given off. ¹	
	Calories.	Per cent. ²	Calories.	Per cent.
EXPERIMENTS MORE DIRECTLY COMPARABLE.				
<i>Average of work and rest experiments. Groups A-F.</i>				
Without alcohol (9 experiments) . . .	2927	100.0	2946	100.0
With alcohol (6 experiments)	2942	100.5	2949	100.1
EXPERIMENTS LESS DIRECTLY COMPARABLE.				
<i>Average of rest experiments. Groups G-I.</i>				
Without alcohol (4 experiments) . . .	2301	100.0	2277	100.0
With alcohol (7 experiments)	2356	102.4	2358	103.5
AVERAGE OF ALL ABOVE EXPERIMENTS.				
<i>Groups A-I.</i>				
Without alcohol (13 experiments) . .	2718	100.0	2723	100.0
With alcohol (13 experiments)	2747	101.1	2752	101.1

¹ Including heat equivalent of external muscular work in the work experiments.

² Of amount oxidized without alcohol.

There was slightly more fuel burned and more heat given off from the bodies of the men when they had alcohol in their diet than when they had the same amount of protein and energy in a diet without alcohol, but with conditions otherwise similar. The differences, however, were very small; in the more directly comparable experiments the excess of fuel burned with the alcohol diet, as measured in calories, was only five parts and that of heat given off only one part in 1000. In the less directly comparable experiments the differences were larger, but still small.

The quantities of total food were generally below rather than above the requirements of the body, especially in the work experiments, as may be seen from Table 4. The general results of experiment imply that under such circumstances the body makes economical use of its food and its reserve supply of material. The fact, therefore, that under these conditions the oxidation of material and radiation of heat were so nearly the same with the rations with and without alcohol add still greater force to the comparison.

Conclusion. — The outcome is that in these experiments, with three different men at rest and at work, when 72 grams of alcohol per day, taken in six doses and furnishing 500 calories of energy, replaced the isodynamic amounts of fats and carbohydrates, the alcohol caused no considerable increase in the amount of heat radiated from the body.

If the alcohol in these experiments had all been taken at one dose, it might have caused the cutaneous vessels to dilate, stimulated the sweat glands (?), and increased the circulation, and thus increased the heat radiation. If there had been enough to cause the ordinary symptoms of intoxication, and especially if it had sufficed to induce the comatose condition for which the expression "dead drunk" is used, and if the men had at the same time been exposed to severe cold, the production of heat in the body might have been retarded, and the radiation increased so as to lower the body temperature by several degrees.

Rapidity of combustion of alcohol in the body.

There is a popular impression that alcohol is burned in the body much more rapidly than ordinary food, and that in consequence not only is the energy resulting from its oxidation wasted, but derangements of bodily functions may result from the rapid combustion of the alcohol. The exact grounds for the belief and the nature of the supposed disturbances we have not seen distinctly stated. Nevertheless, as the impression prevails to some extent, at least, among physicians and physiologists, it seems to demand consideration.

Leaving out of account the unsettled question as to how soon after the ingestion of the alcohol its oxidation begins, the main problem is the rate of oxidation. If it is especially rapid, either one of two results may follow. The oxidation of other materials may go on as usual, in which case the total production of carbon dioxide and heat will be abnormally large; or the oxidation of other substances may be diminished so as to compensate for more or less of the oxidation of the alcohol, in which case the rate of production of carbon dioxide and heat may be little, if any, larger than without the alcohol. The natural test will be found in the measurement of these rates of production. So far as we are aware no adequate tests of this character have thus far been made.

In examining the literature of the subject we have not succeeded in finding any experimental proof that the rate of elimination of carbon dioxide or heat from the body is materially increased or decreased by moderate quantities of alcohol. Satisfactory tests would involve the measurement by short periods, as, for instance, hour by hour. Our own experiments were not planned for this purpose, and the measurements were made generally in six-hour periods. There was nothing in the observations to imply that the rate of production of either carbon dioxide or heat was materially increased either immediately after the ingestion of the alcohol or later.

Part of the heat given off from the body is carried away in water

vapor given off from the lungs and skin, but the larger portion finds its way to the water current, by which it is carried out of the chamber. The rate of flow of this current and its rise of temperature in passing through the chamber thus measure the rate of evolution of heat from the body other than that carried away by water vapor.

The observations of rate of flow and rise in temperature are made every few minutes, and thus show the rate of evolution of the larger portion of the heat.

We have taken the pains to calculate the evolution of heat for hourly periods for three series of experiments, in which the alcohol diet and ordinary diet were compared, viz., Nos. 22-24, 26-28, 29-31. The calculations, however, have been limited to the night periods between 7 P. M. and 7 A. M., because the evolution of both carbon dioxid and heat is much more regular by night than by day, and any disturbance, such as might be caused by the rapid oxidation of alcohol, would be more easily detected in comparing the figures for the experiments with and without alcohol during the night periods.

The results of these comparisons are negative. There are practically no more irregularities or indications of disturbance in the alcohol than in the non-alcohol experiments. There is nothing in the figures which seems to us to indicate any appreciable tendency toward increase of heat production during the first, second, or third hour after the ingestion of the alcohol. The figures are, indeed, so destitute of such indications as hardly to warrant their printing.

The experiments by Chauveau, with dogs, described on page 187 above, accord with the hypothesis that alcohol may not be burned more rapidly than carbohydrates. When the dogs received rations containing meat, sugar, and alcohol, and were put to work in a treadmill shortly after, and the determinations were made of carbon dioxid exhaled and oxygen used, the respiratory quotients implied that the chief material burned during these working periods of one or two hours was carbohydrate, either glycogen or sugar. The respiratory quotients for the remainder of the day implied that the larger part of the alcohol was burned during the ten hours next succeeding the working period. These experiments, which are the only ones of the kind that have come to my notice, are opposed to the theory of the immediate and rapid oxidation of alcohol.

Conclusion.—We are therefore led to the conclusion that in these experiments either the alcohol was not suddenly or rapidly oxidized, or if there was such rapid oxidation, there was a corresponding decrease in the oxidation of carbohydrates, fats, or protein.

It is interesting to note that this conclusion accords with the other observations, viz., those of the total heat production and the economy of

the use of energy in the rations with or without alcohol. All of these imply that the alcohol, carbohydrates, and fats simply replaced one another as sources of energy; that as either was oxidized the others were proportionately spared.

Alcohol as a source of heat in the body.

In the rest experiments the heat given off from the body was equivalent to the total potential energy of the materials oxidized. This was as true in the experiments in which alcohol made part of the diet as in those with ordinary food exclusively. The alcohol must therefore have contributed its full quota of heat as truly as did the starch or fat, and all its potential energy was converted into heat within the body.

In the work experiments the same principle applies, and it follows that unless all the potential energy of the alcohol was converted directly into that of external muscular work part must have been converted into heat within the body. But the total energy of external muscular work was at most the equivalent of 280 calories, while the energy of the alcohol was about 500. Even if all the external work was done at the expense of the alcohol, there would remain 220 calories which must have been transformed into heat within the body. But it is extremely improbable that the alcohol supplied all and the ordinary food none of the energy of external work. In so far, therefore, as the latter came from the ordinary food, more than 220 of the 500 calories of the alcohol must have reached the form of heat within the body.

We have to do here with the question: Of the total energy which was potential in the alcohol and was made kinetic by its oxidation, how much was transformed directly into heat and how much was first changed to the energy of muscular and other bodily work, internal and external, and was afterwards transformed into heat? This involves two fundamental problems. One is the still unsettled physiological question as to whether the production of muscular energy in general is or is not a direct transformation of potential into mechanical energy. The other is the more specific question as to whether the energy of alcohol is like that of the ordinary nutrients of food in its transformation into muscular energy. Both will be referred to beyond in the discussion of alcohol as a source of muscular energy. Meanwhile it is safe to say that—

1. Unless all the potential energy of the alcohol was transformed directly into the energy of internal work in the rest experiments or into that of internal and external work in the work experiments, a supposition that seems highly improbable, part must have been transformed directly into heat in the body.

2. Whether the potential energy was first transformed into muscular energy or not, the whole in the rest experiments, and, in all probability, part at any rate in the work experiments, reached the form of heat within the body.

Conclusion.—It follows, therefore, that in all the rest experiments alcohol was certainly, and in the work experiments it was in all probability, a source of heat for the body.

Alcohol as a source of muscular energy.

General considerations.—The question whether or not the energy of alcohol is used for muscular work is not yet definitely answered. The experiments thus far made do not provide means for tracing the energy of the alcohol through the changes it undergoes in the body, and finding how much of it becomes muscular energy. Nor is it easy to devise such experiments. The difficulty is that the potential energy of the alcohol is transformed along with that of other materials oxidized, and there is no known way of separating the kinetic energy which comes from the alcohol from that which is supplied by the carbohydrates or fats or protein. While there is no evidence of any differences between the energy from the several sources, the absolute proof that no such differences exist is not yet at hand.

Back of this is the more fundamental question as to how muscular energy is produced. Concerning this two theories are held. One is that part of the potential energy of the food and body material oxidized is converted directly into the mechanical energy exerted by the muscle. The other is that the contraction of the muscle, by which its work is done, is due to heat. According to this view, practically all of the potential energy is first transformed into heat and a part afterwards appears as muscular energy. If the second view is correct, it is hard to see how the heat derived from the oxidation of the alcohol should be in any way different from the rest of the heat. If the muscular energy is the first product of the transformation of potential energy, it is conceivable that there might be some attribute of alcohol which would prevent its potential energy from being changed into mechanical energy. But there is nothing in the results of experiment to imply any such difference between alcohol on the one hand, and sugar, starch, or fat on the other. The case regarding the transformation of energy is like that just referred to regarding the use of the energy after it is transformed. There is no evidence of any difference between alcohol and other nutrients in either respect, but there is no proof that the difference does not exist.

If the experiment could be made with lean meat and alcohol in such a way that the body could obtain no other fuel than alcohol and

protein, and the energy of the total muscular work, internal and external, should be found to exceed the energy supplied by the protein, it would be clear that the rest of the muscular energy must come from the alcohol. But as yet we have no means for measuring the internal work, so as to prove that it would be more than the protein could provide for, and it would probably be difficult to find a man who could do much external work day after day on such a diet without drawing upon the store of material in his body.

For the present, therefore, we are limited to experiments in which other fuel is burned with the alcohol, and the difficulty is to prove absolutely that muscular work is done by use of the energy of the alcohol when there is other fuel to supply the energy.

Our experiments simply compare the income of energy from the oxidation of ordinary nutrients and alcohol with the outgo of energy in the different forms of heat and external muscular work, and do not answer the specific question as to how much of the energy provided by the alcohol is used for either internal or external muscular work, or both.

Economy of utilization of the energy of the rations with and without alcohol.—We may nevertheless get some light on the question by putting it in another way: Is the total energy of the ration used as economically when part of it is supplied by alcohol as when the whole comes from ordinary food? The question may be approached in two ways, (1) by considering the amounts of available energy in the diets with and without alcohol, and comparing these with the energy in the body protein and fat gained or lost in the two cases; and (2) by comparing the energy of material actually oxidized in parallel experiments with and without alcohol. The principles here involved may be explained as follows:—

The energy needed and used by the body.—The body requires and uses a certain amount of energy. This amount is larger when the man is at work and smaller when he is at rest. The larger the amount of energy used, the more material will be metabolized to furnish it. If the available nutrients of the food exceed the amounts metabolized, the excess will be stored in the body. Assuming the store of carbohydrates to remain constant, the body will gain protein or fat or both. Translating this last statement from terms of material to terms of energy: if the available energy of the food exceeds the energy metabolized, the amount of energy in the body will be increased by the storage of energy in protein or fat. On the other hand, if the available energy of the food does not supply the demand, the lack will be made up by drafts upon body protein or fat. We thus have two measures of the energy used by the body. One is the

gain or loss of body protein and fat with a given amount of available energy in the food. The other is the total energy metabolized, whether it be more or less than the available energy of the food.

Economy of utilization of energy. — We have distinguished between the energy needed and that actually metabolized. If the body uses the energy economically, it does not metabolize more than it needs. But it does not always make the most economical use of either material or energy. If it has more food than it needs, it may use this wastefully. Part of the excess of material, at times perhaps the whole, may be stored for future use, but often more or less of the excess is simply consumed and the energy wasted. On the other hand, if the food only equals the demand, and especially if it falls short and body material has to be drawn upon, the body will probably make economical use of the energy of both food and body material. This was the case in the experiments now under discussion. When the men were at rest the food supplied but little more, and when they were at work it supplied less, than was actually needed. In these experiments, therefore, the two measures just referred to, namely, the energy of body material gained or lost, and the total energy metabolized, show how much the body uses when the energy is economically utilized.

To state the case in another way, either the energy of material gained or lost with the given diet, or the energy of the total material oxidized, gives a measure of the energy actually employed for economical use. These quantities can be expressed in calories.

Comparative economy of energy of different nutritive materials. — This brings us to the question at issue. Is the energy of alcohol equal, superior, or inferior in value to that of carbohydrates or fats or other nutrients of ordinary food as part of a diet for rest or for muscular work? Will a calorie of energy from alcohol go as far, farther, or not so far as a calorie from sugar, starch, or fat, or protein in meeting the actual needs of the body? The answer is to be sought in the experiments in which a diet of ordinary food is compared with a diet containing alcohol, the total available protein and energy of the food and the other conditions being the same in both experiments. The test will be found in the gains or losses of body protein and fat, and in the total energy metabolized in the two experiments. Any differences in either of these factors, to wit, (1) gains or losses of body material, or (2) energy metabolized, provided they are outside the limits of experimental error, must be attributed to the diet; that is to say, the alcohol in the diet. If the body gains or loses the same amount of material, or if it metabolizes the same amount of energy with both diets, a calorie of energy from one is equal to a calorie of energy from

the other, and as a source of energy the alcohol is equal to the isodynamic amount of the carbohydrates or fats which it replaces. If the gain of material is less or the loss more, or if the total energy metabolized is larger with the alcohol, the latter is inferior as a source of energy, and *vice versa*.

As illustrations we may compare the figures for two pairs of experiments with E. O., as is done in the table herewith.

Comparative gains and losses of body protein and fat, and energy of material oxidized in experiments with and without alcohol.

[Quantities per day.]

	Available in food.		Gain (+) or loss (—) in body material.		Energy of material oxidized in body.
	Protein.	Energy.	Protein.	Fat.	
	Grams.	Calories.	Grams.	Grams.	Calories.
REST EXPERIMENTS.					
No. 9. E. O., ordinary diet . .	112	2426	— 3.6	+ 18.3	2274
No. 10. E. O., alcohol diet . .	115	2427	— 6.7	+ 21.0	2265
WORK EXPERIMENTS.					
No. 11. E. O., ordinary diet . .	110	3510	— 3.0	— 40.1	3909
No. 12. E. O., alcohol diet . .	113	3614	— 1.0	— 32.5	3928

Nos. 9 and 10 were rest experiments. The available (digestible) protein and energy in the food were nearly the same in both. The body lost a little more protein and gained a little more fat with the alcohol than with the ordinary diet, but the differences in gain and loss were very small as compared with the 72 grams of alcohol with its 500 calories of energy. In the work experiments the outcome was similar. The amounts of available protein and energy in the food were somewhat larger with the alcohol diet, but total protein and energy were more nearly equal, the difference being due in part to the less complete digestion of the food of the ordinary diet. The body lost both protein and fat in both experiments, but the differences between the losses with and without alcohol were not large. The comparisons of gain and loss here are complicated by the fact that they consist of both protein and fat. They can be simplified by expressing them in terms of energy corresponding to the protein and fat, as is done in Table 5.

The comparative efficiency of the rations is shown more clearly by the amounts of energy in the material oxidized in the body. In calculating this energy account is taken of both the food eaten and the body material gained or lost. The available protein and energy in the food,

the muscular exercise and other conditions being the same with the alcohol ration as with the ordinary ration, if the energy of the alcohol is not as effective as that of the fats and carbohydrates which it replaced, more energy will be needed by the body to make up the deficiency; but if a calorie of the energy of the alcohol is as effective as a calorie of the energy of fats or carbohydrates, the energy of the material oxidized in the body should be the same with the alcohol ration as with the ordinary ration. In the experiments just cited the energy of the food and body material oxidized is very nearly the same with alcohol as without it. Here again the evidence favors the belief that the alcohol was nearly if not quite equal in actual effectiveness to the isodynamic amounts of carbohydrates and fats.

As a matter of fact these two methods of estimating the effectiveness of the rations, one by the gain or loss of body material and the other by the energy of material oxidized, amount to one and the same thing.

Average results of the experiments.—Table 5 shows the differences between the available energy of the food in experiments with and without alcohol and the corresponding differences between the amounts of body material gained or lost and energy transformed in the averages of all the experiments. The figures in the fourth and sixth columns are computed from those in the third and fifth, respectively, using the factor 5.65 for the energy of one gram of protein, and 9.54 for that of one gram of fat.

TABLE 5. — *Comparison of gains and losses of body protein and fat, and transformation of energy in experiments with and without alcohol.*

[Quantities per day.]

Class, kind, and number of experiments.	Available in food.		Gain (+) or loss (—) in body material.				(g)
	(a)	(b)	(c)	(d)	(e)	(f)	
	Protein.	Energy.	Protein.	Energy of protein <i>c</i> ×5.65.	Fat.	Energy of fat. <i>e</i> ×9.54.	Energy of material oxidized. <i>b</i> −(<i>d</i> + <i>f</i>)
	Grams.	Cal.	Grams.	Cal.	Grams.	Cal.	Cal.
<i>Class I. — More directly comparable:</i>							
9 experiments without alcohol	103	2917	−3.5	−20	+1.0	+10	2927
6 experiments with alcohol . .	104	2925	−6.8	−39	+2.3	+22	2942
Increase (+) or decrease (—) with alcohol	+1	+8	−3.3	−19	+1.3	+12	+15
<i>Class II. — Less directly comparable:</i>							
4 experiments without alcohol	100	2239	−7.2	−39	−2.4	−23	2301
7 experiments with alcohol . .	98	2400	−3.0	−21	+6.8	+65	2356
Increase (+) or decrease (—) with alcohol	−2	+161	+4.2	+18	+9.2	+88	+55

TABLE 5. — (Continued.)

Class, kind, and number of experiments.	Available in food.		Gain (+) or loss (−) in body material.				(g) Energy of material oxidized. $b-(d+f)$
	(a)	(b)	(c)	(d)	(e)	(f)	
	Protein.	Energy.	Protein.	Energy of protein. $c \times 5.65$.	Fat.	Energy of fat. $e \times 9.54$.	
<i>Class III. — Average of I. and II.:</i>	Grams.	Cal.	Grams.	Cal.	Grams.	Cal.	Cal.
13 experiments without alcohol	102	2691	−4.7	−26	−.1	−1	2718
13 experiments with alcohol	102	2750	−5.5	−33	+3.8	+36	2747
Increase (+) or decrease (−) with alcohol	0	+59	−.8	−7	+3.9	+37	+29
<i>Work and rest experiments of Class I.:</i>							
Work experiments compared —							
5 experiments without alcohol	100	3337	−5.0	−28	−31.8	−303	3668
3 experiments with alcohol	100	3361	−9.8	−56	−29.5	−281	3698
Increase (+) or decrease (−) with alcohol	0	+24	−4.8	−28	+2.3	+22	+30
<i>Rest experiments compared —</i>							
4 experiments without alcohol	106	2496	−2.0	−11	+33.8	+322	2185
3 experiments with alcohol	108	2489	−3.8	−21	+34.1	+324	2186
Increase (+) or decrease (−) with alcohol	+2	−7	−1.8	−10	+3	+2	+1

The bold-face figures in the last line of each group in the columns for protein and fat give the gain or loss of material and energy in the alcohol experiments as compared with those without alcohol. The plus sign indicates greater gain and the minus sign greater loss with the alcohol than without it.

The figures in the last column represent the energy of material actually oxidized; that is, the total energy metabolized in the two classes of experiments. The bold-face figures show by the + sign the excess of energy metabolized with the alcohol diet. The values are found by deducting the algebraic sum of the calories of energy gained or lost in protein and fat from the total available energy of the food as indicated by the letters and formulæ in the column headings. Thus in the first group we have an excess of $+8 - (-19 + 12) = 15$ calories of total energy metabolized in the alcohol as compared with the non-alcohol experiments. The same result is found by comparing the total quantities of energy metabolized, namely, 2927 without and 2942 with alcohol. The variations in the amounts of body material gained or lost and in the amounts of energy metabolized in the two classes of experiments may be due to either of three causes.

1. Such experimental errors as irregularities in the daily absorp-

tion of the food from the alimentary canal, or variations in the amounts of carbohydrates in the body which are here assumed to be constant from morning to morning, or from experiment to experiment, or small errors in the estimates of gains or losses of protein and fat from the gains or losses of nitrogen and carbon. These errors are hardly avoidable, but on the whole they appear to counterbalance one another so that their effect is eliminated in the averages of a considerable number of experiments.

2. Differences in the activity of the subjects in the two classes of experiments. These differences are not easy to avoid. The man in the chamber may make more muscular effort on one day than on another in taking down his bed in the morning and in setting it up at night, or he may move about more in caring for the food and excretory products and weighing himself and the absorbers. In the work experiments there may be differences in the external muscular work despite the best efforts to make the amounts constant from day to day. These differences in muscular activity, though small, may affect the metabolism of matter and energy.

3. The energy furnished by the alcohol may not be as efficient, calorie for calorie, in meeting the demands of the body as the energy from the materials which it replaces.

It is hardly to be supposed that the experimental errors in categories (1) and (2) will be considerable. It is still less probable that they will be so concentrated in either the alcohol or non-alcohol experiments as to materially affect the average results. If, therefore, the differences between the figures for the experiments of the two classes are large and reasonably constant, it would seem fair to attribute them to differences in the actual value of the alcohol as compared with isodynamic amounts of fats and carbohydrates. The figures of Table 5 show differences to the disadvantage of the alcohol. The differences are, however, mainly within the range of experimental error.¹

¹ The differences between the results with and without alcohol are in all cases small. Considering them from the ordinary mathematical standpoint, they are, of course, noticeable; but in such physiological experimenting as this the unavoidable errors of individual experiments are considerable, and it is only when a large number of such experiments are averaged that differences of one or two parts in one hundred could properly be regarded as significant. Indeed, in this whole discussion there is danger of being misled by the figures in the tables unless one constantly recalls the fact that the range of unavoidable variation is wide. When, however, the averages of large numbers of experiments show a constant difference on one side or the other, it may be permissible to use such differences for conclusions and generalizations. On the whole, it might seem that in these experiments the results were sufficiently numerous to imply a slight inferiority of the alcohol

In the more directly comparable experiments (Class I.) the conditions with and without alcohol were closely similar. In Class II. there were not inconsiderable differences between the amounts of protein and energy in the diet, in the number of subjects, in the number of experiments, and in the amounts of muscular exercise. These differences do not, in our judgment, destroy the value of the comparisons in Class II., though they do make the differences in result less decisive. The results of Class II. are, therefore, valuable as confirming those of Class I.

Gains and losses of body material as indicative of the relative effectiveness of alcohol. — The differences in the gains or losses of protein and fat in the experiments with alcohol as compared with the others are slightly to the disadvantage of the alcohol. They thus imply that, calorie for calorie, the energy furnished to the body by the alcohol was less effective than that furnished by the carbohydrates and fats. These differences may be due to experimental errors, but even if they are wholly charged to the alcohol they make it only slightly inferior to the nutrients which it replaces. The inferiority is found only in the work experiments; in the rest experiments there is practically no difference between the alcohol and the ordinary nutrients in effectiveness.

Amounts of energy metabolized as indicative of the relative effectiveness of alcohol. — The results here are similar to those found in the comparison of gains or losses of material. This is to be expected, since the two measures are really different expressions of the same fundamental fact. In the rest experiments the results with and without alcohol are practically identical. The inferiority of the alcohol is limited to the work experiments.

The comparisons are brought out very clearly in the discussion of the effect of alcohol upon the radiation of heat from the body on pages 260-262, in which the amounts of energy metabolized in the experiments with and without alcohol are shown. The averages for all the experiments are epitomized herewith.

in respect to the economy of the use of energy; but this inference rests upon the rather questionable assumption of the absolute equality of all conditions other than the presence or absence of alcohol in the diet.

Average amounts of energy in material oxidized.

[Calories per day.]

Classes and groups.	Experiments.	Ordinary diet.	Alcohol diet.
I. { A-C..	More directly comparable, rest.....	2185	2186
I. { D-F..	More directly comparable, work.....	3668	3698
I. { A-F..	More directly comparable, all.....	2927	2942
II. G-I..	Less directly comparable, rest	2301	2356
III. A-I..	All above	2718	2747

It appears that in the more directly comparable experiments the energy of material oxidized averaged the same where the subjects were at rest, but was about 1 per cent. larger with the alcohol when they were at work. In the less directly comparable experiments, in all of which the subjects were at rest, the average was larger by about 2 per cent. with the alcohol diet. This is perhaps no more than was to be expected with the slight differences in the conditions of the experiments.

In this method of comparison by amounts of material and energy oxidized, as in the previous method, the differences were too small to be taken into account in individual experiments, but appearing as they do in the average of a number of experiments they are not without significance. The conclusion is that the energy of the alcohol diet was slightly less economically used than that of the ordinary diet, especially in the work experiments. This implies that the energy of the alcohol itself was less economically utilized than that of the fats and carbohydrates, but the differences are so small as to be of little or no practical consequence.

Relative effectiveness of alcohol expressed in percentages. — In the work experiments of Class I. 3668 calories were metabolized with the ordinary, and 3698 with the alcohol ration. The relative costs of maintaining the body with the two rations were thus $3668 : 3698 = 100 : 100.8$ or $99.2 : 100$; the difference of 30 calories being 0.8 per cent. Assuming the difference to be due wholly to the inferiority of the alcohol ration, its effectiveness, calorie for calorie, would be 99.2 per cent. of that of the ordinary ration, so far as the energy is concerned.

The alcohol supplied 500 calories of energy, of which the 30 calories would represent 6 per cent. If we charge the deficit wholly to the alcohol, the latter would be, calorie for calorie, 6 per cent. less effective than the fats and carbohydrates it replaced. In other words, the effectiveness of the alcohol as a source of energy in the ration for muscular work in this case would be 94 per cent. of that of the isodynamic amounts of carbohydrates and fats.

Calculated in these ways the effectiveness of the alcohol ration as compared with the ordinary ration, and that of the alcohol as compared with carbohydrates and fats in the experiments of Classes I.-III., would be as follows : —

Percentages of effectiveness of energy.

Experiments.		Energy of alcohol ration as compared with energy of ordinary ration.	Energy of alcohol as compared with energy of carbohydrates and fats.
Groups.	Classification.		
		Per cent.	Per cent.
I.	More directly comparable.....	99.5	97.0
II.	Less directly comparable.....	97.7	89.0
III.	Average of I. and II.	99.0	94.2
I.	Rest experiments.....	100.0	99.8
I.	Work experiments.....	99.2	94.0

Summary. — The conditions and results of these experiments and the inferences here drawn from them regarding alcohol as a source of muscular energy may be briefly summarized : —

1. We have here experiments with ordinary diet compared with other experiments in which the conditions were similar except that carbohydrates and fats sufficient to supply 500 calories of energy of the 2200-3600 calories in the daily ration were replaced by the isodynamic amount (about 72 grams) of alcohol, the latter being taken in six doses. The conditions of work and rest were very nearly the same in the corresponding experiments, with and without alcohol.

2. The amounts of material and energy transformed in the experiments with alcohol were very nearly the same as in the corresponding ones without alcohol. Where the ration was insufficient to meet the needs of the body, and it had to draw upon its store of fat and protein to supply the lacking energy, the drafts were practically the same with the ordinary as with the alcohol diet, so far as concerns the energy of the body material drawn upon.

3. The utilization of the energy of the whole ration was slightly less economical with the alcohol than with the ordinary diet, especially when the subjects were at hard muscular work, but the difference in favor of the ordinary food was very small indeed, hardly enough to be of practical consequence. From this it follows that the energy of the alcohol was utilized very nearly or quite as well as that of the other fuel ingredients which it replaced.

Conclusion. — The hypothesis that the alcohol contributed its share of energy for muscular work is natural and extremely probable, but

not absolutely proven. The hypothesis that the energy of the alcohol was not so used is not called for as an explanation of any fact observed in these experiments.

It should not be forgotten that the desirability of alcohol as part of a diet for muscular work is not decided by the narrower questions here discussed. There is a very essential difference between the transformation of the potential energy of alcohol into the mechanical energy of muscular work and the advantage or disadvantage of alcohol in the diet of people engaged in muscular labor. Even with the small doses in these experiments there were indications that the subjects worked to slightly better advantage with the ordinary rations than with the alcohol. The results of practical tests on a large scale elsewhere coincide with those of general observation in implying that the use of any considerable quantity of alcoholic beverages as part of the diet for muscular labor is generally of doubtful value and often positively injurious.¹

The availability and fuel value of alcohol in nutrition.

The experiments give data for comparing the availability and fuel value of alcohol with those of the nutrients of ordinary food. The word availability, as here applied to the ordinary nutrients, expresses the proportion which is digested and made available for the building and repair of tissue and the yielding of energy. This proportion is the difference between the total amount and that excreted as feces by the intestine.

In like manner the available alcohol would be the difference between the total amount ingested and the amount excreted by the lungs, skin, and kidneys, practically none being excreted by the intestines.

Alcohol does not require digestion, no part of it is excreted by the intestine under ordinary conditions, it is completely "digestible," but part escapes by the kidneys, lungs, and skin. The rest is oxidized and is available for yielding energy.

The available energy of the ordinary nutrients, *i. e.* the energy the body can utilize, like that of alcohol, is the total energy (heat of oxidation) less that of the material unoxidized. For fats, carbohydrates, and alcohol, it is the heat of oxidation of the total available material. For the protein it is the same less the heat of oxidation of the unoxidized residue excreted by the kidneys. The available energy is taken as the measure of the fuel value.

The proportion of nutrients and energy which are thus available,

¹ For a summary of results of experiments upon various phases of this subject by different investigators, see article by Prof. J. H. Abel in this volume.

when expressed in percentages, are called coefficients of availability. Thus it is found that about 97 per cent. of the carbohydrates of ordinary diet are available, hence 97 is taken as their coefficient of availability. Table 6 herewith compares the coefficients of availability and the fuel values of the protein, fats, and carbohydrates of ordinary diet, as found by a considerable number of experiments,¹ with those of alcohol as shown by the experiments here reported. The heats of combustion are as found by burning the materials with oxygen in the laboratory by use of the so-called bomb calorimeter. The fuel values, as given in the fourth and fifth columns, represent the energy yielded to the body by a gram or a pound of available material; those in the last two columns express the amounts of energy the body can obtain from the given quantity of total materials, and hence are more convenient for ordinary use. Thus a gram of protein, when completely burned with oxygen in the bomb calorimeter, will yield on the average, 5.65 calories of energy. When it is metabolized in the body, however, the oxidation is not complete. In the first place the equivalent of about 8 per cent. of the protein of ordinary diet is excreted in the feces, so that only 92 per cent. can be utilized by the body to build tissue and supply energy. The coefficient of availability of the protein is hence taken at 92. When this available protein is broken down (katabolized) in the body, the larger part is oxidized, and its energy is made available, but the oxidation is not complete, since a certain portion is excreted by the kidneys in urea and other compounds, which still contain potential energy. It is customary to take the heat of combustion of the unoxidized material of the urine as a measure of the energy which remains in this unoxidized material and is not utilized by the body. Subtracting this unavailable energy from the total energy of the available protein, leaves the available energy. Enough energy is thus lost to make about 24 per cent. of the available protein, or 22 per cent. of the energy of the total protein.

¹ See discussion of this subject by W. O. Atwater and A. P. Bryant in the *Report of the Storrs (Conn.) Experiment Station for 1899*, from which the figures for ordinary nutrients in the table are taken. The original data are found in the results of analyses of over 4000 specimens of American food materials; several thousand determinations of food materials and excretory products; some 350 studies of dietaries of several thousand people of various classes in different parts of the United States, and not far from 300 digestion experiments, mostly with men; a considerable number of metabolism investigations, including 30 experiments, covering 93 days, with men in the respiration calorimeter, and a not inconsiderable amount of other inquiry. The larger part of this work was done in the writer's laboratory and elsewhere, in connection with the general inquiry referred to in the text on page 174.

Adding the 8 per cent. of whole energy of the protein lost in the feces, the total loss of energy is estimated at 30 per cent. and only 70 per cent. can be actually utilized; accordingly the coefficient of availability of the energy of the protein is 70.

TABLE 6. — *Comparison of availability (digestibility) and fuel values of nutrients of food in ordinary diet with those of alcohol.*

	Heat of combustion per gram.	Coefficients of availability.		Fuel values.			
		Of material.	Of energy.	Referred to available material.		Referred to total material.	
				Per gram.	Per lb.	Per gram.	Per lb.
	Calories.	Per cent.	Per cent.	Calories.	Calories.	Calories.	Calories.
Protein . . .	5.65	92	70	4.4	2000	4.0	1815
Fats	9.40	95	95	9.4	4260	8.9	4040
Carbohydrates	4.10	97	97	4.1	1800	4.0	1818
Alcohol . .	7.07	98	98	7.1	3210	6.9	3130

To state the case in another way: of the 5.65 calories of energy in the gram of protein 1.65 calories escape in the unoxidized material of feces and urine, and the remaining 4 calories, which are available, represent the fuel value.

Of the fat the equivalent of about 5 per cent. is given off in the feces, and the rest is completely burned. Accordingly 95 per cent. of the fat itself and the same proportion of the energy are available, and as the total energy or heat of combustion of a gram is 9.4 calories, the fuel value is estimated to be 8.9 calories. In the same way the available material and the available energy of the carbohydrates are estimated at 98 per cent., and the fuel value is 4.0 calories per gram.

A gram of alcohol, when completely oxidized, yields 7.07 calories of heat, but when alcohol is taken into the body in moderate doses, about 2 per cent. escapes oxidation and is given off through the lungs, skin, and kidneys. The remaining 98 per cent. is oxidized and yields 6.9 calories of energy, which is the fuel value of the gram of alcohol.

A gram of available material would yield more energy than a gram of total material, as shown in the fourth and fifth columns of the table.

It is to be remembered that the figures of the table are general averages; the proportions would differ more or less in individual cases.

Isodynamic values. — A gram of alcohol thus yields 6.9 calories, and a gram of carbohydrates 4 calories. On this basis it would require $(6.9 \div 4 =) 1.73$ grams of carbohydrates to furnish the 6.9 calories

supplied by the gram of fat, or, in technical phrase, 1.73 grams of carbohydrates are isodynamic with 1 gram of alcohol. In like manner, as the fuel values of alcohol and fat are as 6.9 to 8.4, 0.78 grams of fat would be isodynamic with the gram of alcohol. Speaking roughly, 1 gram of alcohol, $1\frac{3}{4}$ grams of carbohydrates, and $\frac{3}{4}$ gram of fat yield the same amounts of energy to the body, and hence are isodynamic with each other.

Other views.—The theory has been suggested that the kinetic energy furnished by alcohol differs in quality from that which comes from the ordinary nutrients. Thus Dastre¹ designates such compounds as carbohydrates and fats as *biothermogens*, and others, such as alcohol, glycerine, and the organic acids as *pure thermogens*; the distinction being that the energy coming from the oxidation of the biothermogens can and that from the pure thermogens cannot be utilized by the body. In adopting this theory Dastre appears to have followed the inference which has been drawn from the experiments of Miura and others, that alcohol cannot protect body protein from consumption. It may be that the theory held by some physiologists to the effect that any substance in order to serve the body as nutriment must first become an integral part of living proteid or protoplasm, seems also to be made by Dastre a basis of his theory. The hypothesis is certainly an interesting one and may be very attractive if one accepts the beliefs upon which it seems to rest. But these beliefs are opposed by such late experiments as those of Neumann, Clopatt, Rosenfeld-Chotzen, and Rosemann, which show that alcohol can and does protect protein.² They are also opposed to our own experiments in which rations with and without alcohol, but alike in available protein and energy, were equally efficient in protecting body material both when the subjects were at rest and when they were at work.³

In like manner Kassowitz designates alcohol, glycerine, and the organic acids as *werthlose Brennstoffe*, useless fuel. His opinion apparently rests upon grounds similar to those taken by Dastre as just stated.⁴

General considerations.—Aside from the question of the power of

¹ Vol. i. of this Report, page 79.

² See pages 198–204.

³ See pages 252–259.

⁴ See above. In an article which has appeared since this was written (Pfüger, *Archiv. f. d. ges. Physiol.* 90, 421), Kassowitz attempts to show, from some of the European experiments summarized in the preceding pages, especially those of Chauveau, that alcohol neither protects body material nor yields useful energy to the body, that indeed it has no nutritive value and is only a poison.

alcohol to protect protein and fat and supply energy to the body for various useful purposes, there are the weightier considerations of the general effect of alcohol upon the muscular, and especially the nervous system, and upon health and welfare. Upon these most serious hygienic, economical, and ethical problems, the experiments here reported throw no special light.

CHAPTER IV.

THE FOOD-VALUE OF ALCOHOL.

HAVING thus described our experiments, the summarizing of the plan and results is a comparatively simple matter. The just interpretation of the results is a far more difficult task. The conclusions here stated are those to which I have been led by considering, in connection with the Middletown investigations, the published results of the work of the leading experimenters in this country and in Europe, especially those cited in the preceding chapter and by personal conversations with a not inconsiderable number of such investigators and other authorities upon the subject. In presenting the conclusions, it has seemed best to enlarge their scope and include a number of general considerations bearing upon the subject of the nutritive value of alcohol.

The Middletown experiments : purpose, subjects, and method.

The purpose of these experiments, so far as the physiological action of alcohol is concerned, was primarily to get light upon the ways by which its potential energy is transformed and utilized in the body, but attention was also given to the effects of alcohol upon the digestion of the food taken with it, the proportions of alcohol that were oxidized and escaped oxidation, and its effects upon the metabolism of carbon and nitrogen and the gain and loss of fat and protein in the body.

The subjects were three young, healthy, active men who were ordinarily engaged in rather light work ; one was a laboratory assistant, one a physicist, and one a chemist in the chemical laboratory of Wesleyan University, where the experiments were made. The first, E. O., a Swede by birth, had been accustomed from his youth to drink small quantities of alcoholic beverages ; the other two, A. W. S. and J. F. S., had always been abstainers.

The results of experiments with ordinary diet were compared with those of experiments in which part of the fats and carbohydrates of the ordinary food were replaced by the isodynamic amount, about 72 grams ($2\frac{1}{2}$ ounces) of absolute alcohol per day, generally in the form of commercial alcohol, though in one experiment brandy and in another whiskey was used. The amount of alcohol was about as much as would be supplied in a bottle of claret or Rhine wine, or 6 ounces of whiskey, or 5 ounces of brandy. It was taken in six nearly equal doses, three with meals and three between meals.

The ordinary diet consisted of meat, milk, bread, cereals, butter, sugar, and the like, with, in some cases, coffee. The quantities were such as had been found to be sufficient, or nearly so, for meeting the demands of the body under the conditions of the experiments, whether of rest or muscular work. The methods of preparation were such as to make the food palatable to the subject.

During the metabolism experiments proper the subjects were in the chamber of the respiration calorimeter, where they remained during periods varying from 4 to 9 days. The sojourn was made comfortable, and the conditions seemed to be normal. Each metabolism experiment or series of experiments in the respiration chamber was preceded by a period during which the subject had essentially the same diet and nearly the same amount of muscular exercise outside the chamber. In these preliminary experiments the amounts, composition, and heats of combustion of the food, feces, and urine were determined. In the metabolism experiments the determinations include besides these the water and carbon dioxide of the incoming and outgoing air current by which the chamber was ventilated, the heat given off from the body, and, in the work experiments, the heat equivalent of the muscular work done. In the alcohol experiments the determinations were made of the small amounts of alcohol excreted by the kidneys, lungs, and skin.

Accordingly the data of the metabolism experiments show the income and outgo of the body as expressed in terms of (*a*) nitrogen, carbon, and hydrogen; (*b*) water, protein, fats, carbohydrates, and mineral matters; (*c*) potential energy of food and unoxidized excreta; and (*d*) kinetic energy of heat given off from the body and external muscular work performed. The

accuracy of the apparatus and method were assured by burning alcohol within the chamber, measuring the amounts of carbon dioxide, water, and heat produced. Such tests were made generally between each two experiments or experimental series. Taking the theoretical amounts at 100, the average amounts found were carbon dioxide, 99.6; water, 100.6; heat, 99.9.

In the so-called "rest" experiments the subject had no more muscular exercise than was involved in dressing and undressing, weighing himself, arranging his folding bed, chair, and table, and caring for the food and solid and liquid excreta. His diversion was found in reading, writing, and occasional conversation by telephone with persons outside. In the "work" experiments the subject engaged in the active muscular exercise of riding a stationary bicycle for eight hours or thereabouts per day. The wheel of the bicycle was belted to a dynamo connected with an electric lamp, so that the muscular power which was applied to the pedals was converted partly into heat by friction, but mainly into electrical energy and then into heat. The apparatus was calibrated so as to serve as an ergometer for measuring the external muscular work.

In interpreting the results in their bearing upon the physiological action of alcohol, it should be particularly noted that the whole amount of alcohol ingested per day was small, and that furthermore it was taken in 6 doses, 3 with meals and 3 between meals. The object of the experiments was to study the action of alcohol under conditions calculated to secure the minimum of influence upon the nervous system. With such small doses, the equivalent of a glass of wine each, and thus distributed, two of the subjects were able to detect practically no sensible effect of the alcohol, while the third, J. F. S., felt nothing more than at times a slight "tingling" in the ears. There was in some cases an apparent though slight quickening of pulse rate, but practically no lowering of body temperature was observed. In such freedom from nervous disturbance it was believed that the normal nutritive action would be best observed.

There is the more reason for emphasizing this last point, because in the majority of the published experiments with men and animals for the study of the effects of alcohol the quantities of the latter have been much larger. Doses of 1 to 1½ grams per kilogram of body have commonly been considered

small, and those of 2 to 3 grams per kilogram have been common and generally taken on an empty stomach. Often the amounts have been such as to cause the symptoms of drunkenness; in some instances, they have been so large as to be decidedly toxic and even fatal. In our experiments, on the other hand, the whole amount per day was only about 1 gram per kilogram body weight; the individual doses were only about one sixth of a gram per kilogram, and half of them were taken with meals. This fact doubtless accounts for a not inconsiderable share of the difference between the results of our experiments and those found by a number of other investigators.

While the quantities of alcohol were small, the energy sufficed to make about one fifth of the total energy of the diet in the "rest," and one seventh of the total energy of the diet in the "work" experiments.

Limitations of the experiments and of the present discussion.

It is to be especially noted that these experiments were not made to test the effects of alcohol upon muscular or nervous activity or power, nor do they lead to any conclusions regarding the effects of alcohol when taken habitually or in large quantities.

In discussing the physiological action of alcohol and alcoholic beverages, two distinctions should be carefully considered, namely, that between the effects of large and small quantities and that between its action as food and as drug.

Effects of large vs. small quantities of alcohol.

Large quantities produce serious disturbances of bodily and mental functions. Their immediate effect is what we commonly call intoxication. The injury which comes from long-continued and excessive use of alcoholic beverages is so well known and so disastrous as to require no explanation or comment here. I refer, therefore, only to the action of what may be called moderate doses, such as cause no apparent disturbance of the nervous system.

Alcohol as food and as drug.

It is also important to distinguish between the nutritive action of alcohol and the pharmacodynamic action which is

exercised either directly upon cell tissue or primarily on the nervous system, and through that agency or otherwise upon transformations of matter and energy, upon mental and muscular activity, and upon the nutritive functions generally. It will, perhaps, make the distinction clearer if we speak of alcohol as a food and as a drug. This distinction in terms cannot always be made in fact, but it will serve our present purpose.

We may say roughly that alcohol in moderate quantities serves to a limited extent as food, that in large quantities it is clearly a poison, and that in some cases it may be both. This statement, however, is too general to be satisfactory.

It is desirable, therefore, to consider the transformation which alcohol and its potential energy may undergo in the body and the different ways in which its action is exercised. We have to do here chiefly with its nutritive action, and can therefore make only the briefest reference to its pharmacodynamic action, which, taken in the broader sense, is much more important than its action as food.

Effect of alcohol upon digestion.

This may be considered from two standpoints, the influence upon the secretion of the digestive juices and the consequent digestion of food in the alimentary canal, and the influence upon the proportion of nutrients absorbed from the alimentary canal, taken into the circulation and made available for use in the body. From the first standpoint, the subject has been fully discussed elsewhere by Professor Chittenden.¹ It will suffice here to say that alcohol may either retard or accelerate the flow of the digestive juices. Whether alcohol will thus help or hinder digestion in a given case is believed to depend upon a variety of conditions such as the amount of alcohol taken, the form, *i. e.* whether in wine, beer or distilled liquor; the dilution; the food or drink taken with it, and the individuality and state of health of the person. Not enough is now definitely known about the subject to lay down hard and fast rules, but it is certain that large enough doses may materially retard the secretion or the action of digestive fluids, and it is commonly believed that when taken in small amounts and in diluted form, alcohol may at times render very useful aid to enfeebled digestion.

¹ In volume i. of this Report.

The influence of alcohol in moderate quantities upon the amounts of nutrients, *i. e.* protein, fats, carbohydrates, and mineral matters, absorbed from ordinary food, and thus made available to the body for the building of tissue and yielding of energy, does not appear to be very large. The statistical results of our experiments, which are more detailed than any others that have come to my notice, show very little effect of alcohol upon the availability of food in this sense. In some cases, the available protein has been slightly more with alcohol than without, but the differences are too small and too irregular to warrant the conclusion that alcohol generally increases the digestibility of protein.

Amount of oxidation.

Taken in moderate quantities, alcohol is oxidized in the body as completely as ordinary food materials. This subject has been studied by a number of experimenters. In examining the literature of the subject, my associates and myself have found some eighteen investigations of considerable importance, of which the first was in 1846. The authors of one of the earlier investigations, Lallemand, Perrin, and Duroy, in 1860, interpreted their results as showing that alcohol is not burned in the body to any extent, but is given off, unoxidized, through the kidneys, lungs, and skin. This interpretation was speedily shown to be erroneous. What the experiments did show was that very small proportions of the whole alcohol escaped oxidation in the body. Another investigation was thought by its author, Subbotin, in 1871, to show that alcohol is only partially burned in the body. But in his experiments, which were made with rabbits, the doses were very large (equivalent, in one instance, to 13 ounces of strong brandy for a man), so that they had at times to be administered through an incision into the œsophagus, and were, in several instances, fatal. Under these circumstances, the author estimated that at least 16 per cent. of the alcohol ingested was given off, unoxidized, during the first 24 hours. He inferred that, in general, but little alcohol is burned in the body. The incorrectness of this inference was speedily pointed out by other experimenters.

Each of the other sixteen investigations indicated that when alcohol is taken in ordinary doses, the most of it is burned.

Since 1870 or 1875, the only question among physiologists of authority has been as to the completeness of the oxidation, and the more accurately the tests have been made, the smaller have been the proportions found to escape oxidation.¹

In our experiments, on the average, over 98 per cent. of the alcohol was burned, and less than 2 per cent. escaped. While these figures represent the observed results, there is reason to believe that 99 per cent. would more nearly represent the proportion actually oxidized.

I refer thus to the history of this subject, because the theory that alcohol is not oxidized, and hence cannot serve a useful purpose in the body, has, until very lately, been a prominent feature of the so-called "scientific temperance instruction" in our schools.

Rapidity of oxidation of alcohol.

It is sometimes maintained that alcohol is burned in the body so soon after ingestion or so rapidly that it can have little or no nutritive value. I have found no ground for this view, however, except the fact that it is very inflammable, *i. e.* readily oxidized substance.

¹ The following is quoted from Anstie (1874) in a review of the subject by Dr. J. W. Warren in the *Boston Medical and Surgical Journal*, July 7 and 14, 1887 :—

"I therefore trust that we may consider one important portion of the alcohol question to be closed. It is certainly rather hard that the very inadequate researches of Lallemand, Perrin, and Duroy should have been allowed so long to mislead the majority of the profession and of the public upon the subject of the elimination of alcohol, being, as they were, mere qualitative experiments, and, even as such, devised and carried out with such an absence of all reasonable precaution against fallacy, as should have set physiologists on their guard at once. As it is, it has cost some fourteen years of almost unintermittent work to explode the errors which the French observers made current respecting a merely preliminary investigation into the action of alcohol. I appeal to the respectable members of the teetotal party, and I put it to their sense of honor not to continue to circulate the gross misstatements on this subject which, even now, are circulated broadcast in the tracts with which their society floods the country. It cannot do the temperance cause any good in the end; indeed, the discovery that they have been systematically misled on a point as to which their informers could have no difficulty in ascertaining the truth has already produced a strong revulsion in the minds of many persons against everything that bears the more distant relation to teetotalism."

In experiments by Chauveau with dogs,¹ which had alcohol with meat and sugar, the respiratory quotient (ratio of oxygen used to carbon dioxide given off in respiration) implied that during the first one or two hours after the meal, carbohydrate in the form of sugar or glycogen was the principal material burned, and that the most of the alcohol was oxidized during the following ten or twelve hours.

In our experiments at Middletown, no results were found to imply that the combustion of the alcohol was especially rapid. In several cases, the rate of evolution of heat from the body during the first few hours after the taking of alcohol was compared with the rate under conditions otherwise similar, but without alcohol, and was found to be practically the same. If, therefore, the alcohol was oxidized more rapidly than the carbohydrates, fat, or protein in the body, these latter nutrients must have been burned enough more slowly to make up for the rapid burning of the alcohol. The inference was that the body burned material as fast as needed and no faster, whether the ration contained alcohol or not. This corresponds with the fact referred to beyond, that the total oxidation and heat production per day were practically the same with alcohol as without it, provided the rations supplied the same amounts of protein and energy.

There were no indications that the alcohol was burned any more rapidly than the sugar or starch, nor was there anything to imply that it had any other effect upon the consumption of oxygen or production of carbon dioxide than would naturally follow from its being oxidized in the same way as the ordinary nutrients of food; the evidence of the experiments on these points, however, is negative and not conclusive.

The theory of the rapid combustion of alcohol in the body has been strongly urged by some writers as the basis of argument against the nutritive value, but I do not now recall having seen it upheld by any prominent experimenter upon this especial subject.

¹ See p. 187.

Effect of alcohol upon the consumption of oxygen and production of carbon dioxide in respiration.

It has been held by some of the most reputable experimenters and writers upon the subject that alcohol tends to prevent the normal action of oxygen in the body, and thus reduces the production of carbon dioxide. Other authorities have maintained with equal force and candor that it tends to increase the oxidation of carbon and production of carbon dioxide. Both of these opposing theories have been enforced by experimental results which have seemed to their authors and to fairminded students more or less convincing.

In the light of the latest and most reliable inquiry, the conflict is easily explained. It really belongs to a period when the methods of studying the metabolism of matter and energy in the body were far more crude, and the extent to which alcohol is oxidized and the results of its oxidation were not as well understood as they are to-day. In consequence, many of the experiments were defective in plan and execution, and the inferences from some of even the best were such as would not now seem justifiable. Two simple principles, which are to-day reasonably well established, suffice to clear up practically the whole difficulty. One is that alcohol is oxidized in the body like sugar, starch, and fat, and like them yields energy, thus serving as fuel. The other is that, under ordinary conditions, the body burns the fuel at its disposal in quantity sufficient to supply the energy it needs for warmth and work. If part of the fuel is alcohol, there may be either more or less of oxygen used or of carbon dioxide produced, according to the amounts of alcohol or other material burned. This follows from the differences in the proportions of carbon, hydrogen, oxygen, and potential energy of the starch, sugar, fat, protein, and alcohol used as fuel. The quantity of oxygen used or of carbon dioxide given off in the respiratory products may thus be increased or decreased in a wholly natural way.

The theory that alcohol prevents the needed oxidation of food or body material, and thus interferes with a normal function, once seemed plausible, and has played a prominent rôle in the discussions of the last two or three decades, but it is really without foundation.

Transformation of the energy of alcohol. Law of the conservation of energy.

When alcohol is burned in the body, its potential energy becomes kinetic, as is the case with the energy of ordinary food materials. The energy of the alcohol is transformed into heat, and probably into muscular energy also. It leaves the body in the form of heat, except in so far as it may be used for external muscular work. The transformation of the energy of alcohol in the body occurs in accordance with the law of the conservation of energy.

This fundamental principle is reasonably well established by late research. In its various applications are found clear and simple explanations of numerous forms of action of food which were formerly mysterious and misunderstood.

Alcohol as a source of heat for the body.

In the Middletown experiments the amounts of food and body material burned in a man's body, in a given time, as, for instance, a day, are measured, and the amounts of heat which should be produced by their oxidation are determined. The heat given off from the body is also measured. In the rest experiments, *i. e.* those in which the man does no (external) muscular work, the heat given off from the body is found to be just equal to that which must come from the oxidation of the material burned in the body, that is to say, the heat which the body gives off corresponds to the energy which was latent in the food or food plus body material actually burned. This accords with the law of the conservation of energy, and shows that all the energy of the oxidized material was changed to heat in the body. Some of this energy was used for internal muscular work, *e. g.* to keep the heart beating, the blood circulating, and the organs of respiration going, but it was all transformed into heat before it left the body, as is shown by the fact that the heat which the body gave off was exactly equivalent to the total potential energy of the materials burned. In the "work" experiments, the man rode a bicycle-dynamo, and the energy used in driving the machine was changed into heat, and its quantity determined at the same time. The experiments thus showed the amounts of energy given off by the body as

heat and the heat equivalent of the external muscular work. Here, again, the total heat was equivalent to the total energy of the material burned in the body.¹

This brings us to the point. The results were the same when the ration contained alcohol as when it had only ordinary food. Accordingly, the energy latent in the alcohol must have been changed to heat in the body in the rest experiments and to heat or heat and muscular work in the work experiments. The alcohol was therefore a source of heat as truly as the sugar, starch, or fat. This was the case in each and all the experiments. There is every reason to believe that it is generally the case when moderate quantities of alcohol are taken.

Is the heat supplied by the alcohol utilized or wasted?

It is often held that although the latent energy of alcohol is made active in the body, it is wasted and not used. One common argument is this: alcohol so acts upon the nerves which control the blood vessels that an extra amount of blood is brought to the surface of the body and cooled, and more heat is thus radiated from the body. Some go so far as to say that the heat thus lost from the body of the drinker equals or exceeds that supplied by the alcohol.

This theory rests upon two kinds of evidence which make it very plausible. One is the distension of the blood vessels which cause the flush of the skin when alcohol is taken. The other is the lowering of the temperature of the body, which is shown by numerous observations and is explained by the loss of heat. But when we come to examine into the matter closely, we find that although the temperature of the body falls considerably after very large doses of alcohol have been taken, and especially under exposure to great cold, the effect of ordinary doses is slight and often too small to be measured by an ordinary clinical thermometer. When, further, we take pains to calculate how much heat the body would have to lose in order to reduce its temperature as much as is done with a bottle of wine or one or two glasses of whiskey, we find that it would correspond to only a small fraction of the heat which the alcohol yields to the body.

The difficulty with the discussion of this question hitherto

¹ See details of the experiments in the previous chapter.

has been the lack of experimental test. Such tests are found in the Middletown experiments.

If part of the fuel is wasted, more will be needed. If the body has just enough to meet its requirements in the ordinary diet and we take out part of the fat, starch, and sugar, and use the isodynamic amount of alcohol in their places, the ration will furnish the same amount of protein and energy as before. If the bodily activity also remain the same with the alcohol ration, and the alcohol causes a waste of energy while the same energy is demanded as before, then the waste must be made up. This would naturally mean an extra draft upon the body material, that is, a greater loss or smaller gain of protein and fat. The material most drawn upon under such circumstances is fat. In our experiments, the gains and losses of body material were very nearly the same with the alcohol rations as with the corresponding rations without alcohol. This implies that the energy of the alcohol ration was utilized just about as well as that of the ordinary food and opposes the theory that the alcohol greatly increases the heat radiation.

A more direct test, however, is found in comparing the amounts of heat actually given off from the body in the experiments with and without alcohol. Here again the Middletown experiments give extensive data for comparison. In these the results of thirteen experiments with alcohol are compared with those of a like number without alcohol. In some instances, there was more heat radiation, and in others there was less with the alcohol than without it. Such variations are common in physiological experimenting. Taking the extreme cases, there was one in which the heat given off from the body in a day was 45 calories less and another in which it was 55 calories more with the alcohol than without it. Taking all the experiments together, the average daily amount of energy given off from the body with the ordinary diet was 2723 calories, and with the alcohol 2752 calories. If, however, we omit a few of the experiments in which the conditions were slightly different, especially because of differences in the amounts of muscular work performed, and take only those experiments which were strictly comparable and were thus a fairer test, we have six experiments with alcohol to compare with similar ones without it. In these

the heat¹ given off from the body with ordinary diet averaged 2946 calories, and with the alcohol, 2949 calories. The difference, 3 calories, is a trifle over one tenth of one per cent. of the total amount of energy radiated, and about six tenths of one per cent. of the total energy, 500 calories, supplied by the alcohol. These differences come far inside the limits of experimental error.

In the discussion of this subject, confusion often results from failure to distinguish between the heat generated in the body and the temperature of the body. The body has the power of regulating its temperature, chiefly by changes in the rate at which it gives off heat, so that the heat is eliminated as fast as it is produced, and thus the temperature remains nearly constant. Alcohol, when given in large enough quantities, disturbs this regulation and causes an increased radiation of the heat, so that the temperature of the body falls. At least this is the view generally accepted by physiologists. But with small doses of alcohol, such as a moderate drinker would ordinarily take, the fall in temperature is very slight, if, indeed, there be any at all. Under ordinary circumstances, it would take a considerable dose to lower the body temperature by half a degree Centigrade or one degree Fahrenheit. When the doses of alcohol are so large as to make the person "dead drunk," and especially when the body is also exposed to great cold, its temperature may fall several degrees.

To recapitulate: In the Middletown experiments, which were made with three different men, of whom one had been all his life a moderate drinker, and the others were total abstainers, two and a half ounces of alcohol per day, taken in six doses, caused almost no increase in the radiation of heat from the body. Furthermore, the body temperature, as indicated by the clinical thermometer, was very nearly the same with the alcohol as without it.

These facts are opposed to the current theory that alcohol wastes more heat than it furnishes. This theory is based upon the fact that alcohol often does reduce the body temperature. The difficulty is that it leaves the exact statistics out of account. It does so because the statistics have not hitherto been

¹ Including the heat equivalent of the muscular work in the work experiments.

available. Now that we have them, they show the error of the theory.

The theory that the energy yielded by alcohol is lost by the increased heat radiation, like the theories that alcohol is not oxidized in the body, and that it prevents normal oxidation of other material, was suggested by observed facts. In each case, the facts were suggestive but not conclusive. Under crucial tests they are found to fail.

Alcohol as a source of muscular energy.

It is thus clear that alcohol can and does supply heat to the body. It seems probable that it also yields energy for muscular work, but to prove this is not easy. The difficulty is to make experiments in such a way as to show conclusively that the energy used by the muscles comes from the alcohol and not from other materials of either the food or the body itself. We experience the same difficulty in experiments with ordinary food materials. When a man lives upon an ordinary diet, the proteids, fats, sugar, and starch are used together for fuel, and we cannot say just what the body does with the energy of each. But experiments show that when the muscular work is increased, the body generally increases its consumption of fats, sugar, and starch more than the consumption of protein, and we infer that the fats and carbohydrates are its chief fuel materials for the production of muscular energy, as well as for the production of heat.

Fifty years ago, Liebig, the father of physiological chemistry, maintained that the body obtains its heat from the fats and carbohydrates and its muscular power from protein. Later research has led most physiologists to believe that each one of these three classes of nutrients can supply both heat and muscular power, but that the carbohydrates and fats are the chief sources of both heat and muscular power. This view is supported by practical experience. Nevertheless it was only eleven years ago that a leading German physiologist, Pflüger,¹ came out with a vigorous defense of the old theory that the body gets its muscular power mainly from proteids.

Liebig classed alcohol with sugar, starch, and fat as a source

¹ Pflüger, 1891, "Die Quelle der Muskelkraft," *Arch. f. d. ges. Physiol.* l. 98 and 330; and li. 317.

of heat. Later research implies that like them it may furnish both heat and muscular energy. But practical experience indicates that it is a poor food for muscular work.

The experimental evidence regarding the power of alcohol to supply muscular energy is mainly of three kinds: (1) Experiments on a small scale and during short periods in which the strength of the muscle and the resistance to fatigue are observed. (2) Experiments on a large scale, with considerable numbers of men or with animals, during longer periods, in which the work done and the endurance are tested. (3) Metabolism experiments. Those of the first two classes have been reported upon by Professor Abel in the present volume of this Report. Those of the first class include tests with a man's finger, with a frog's muscle, and the like. The results are conflicting and hardly decisive as to the specific question whether the energy of alcohol is or is not converted into muscular work. Indeed they are hardly calculated to settle this question completely. Those of the second class include experiments with soldiers on a march or in a severe campaign; they imply that the men are in general better off without alcohol during the time of strain, though some observers think that a small quantity may be useful for its psychical or psycho-physical action after the work is done. The experiments of this class throw little or no light upon the question as to the transformation of the energy of alcohol into that of muscular work.

Of the respiration experiments, aside from ours, the most extensive with which I am familiar are those of Chauveau with dogs, described above. The animals received a morning meal and were shortly thereafter put into a respiration apparatus for periods lasting from one to two hours, during which time they worked a treadmill. Parallel experiments were made with and without alcohol. The ration without alcohol consisted of lean meat and sugar. In the corresponding alcohol experiments, part of the sugar was replaced by the isodynamic amount of alcohol. The doses amounted to 48 grams of absolute alcohol, and as the dogs weighed about 18 kilograms, these would correspond to 187 grams or $6\frac{1}{2}$ ounces of absolute alcohol as a dose for a man of 70 kilograms or 154 pounds weight. It is not surprising that with such large quantities of alcohol the dogs did less work than when they had the ration without alcohol.

As stated in the reference to these experiments on pages 187-189, above, the respiratory quotient implied that the material burned in the body during these periods of work was largely carbohydrate. How much of this carbohydrate was glycogen or glucose previously contained in the body, and how much was sugar of the meal immediately preceding the period of work, the experiments do not show. The figures for the alcohol experiment are such as would be expected, if a small part of the alcohol were burned during the period of work, and the larger part of the rest were burned during the following ten or twelve hours. It would appear, therefore, that in these experiments, the action of the alcohol during the working period was more pharmacodynamic than nutritive, and that the alcohol in the doses given was much inferior to sugar as part of a ration for muscular work.

The Middletown experiments come closer to demonstrating, though they do not fully prove, that the energy of the alcohol was converted into muscular energy. What they do show is the comparative economy in the utilization of the energy of ordinary food and alcohol. Experiments with ordinary food are compared with experiments similar in the quantities of protein and energy of the ration and in the amount of external muscular work done, but differing in that enough fats and carbohydrates of the ordinary food to yield from one seventh to one eighth of the total energy of the ration was replaced by an isodynamic amount of alcohol. The relative efficiency of the two rations was tested by comparing the amounts of fuel burned and the losses of body material. The larger the amounts of food or body material burned in the body, the less economically is the energy of the ration utilized. The alcohol rations proved slightly inferior, but the average difference, expressed in terms of energy, was equivalent to only about 0.5 per cent. of the energy of the whole ration, or 3.0 per cent. of the energy of the alcohol. The fact that the energy of the alcohol ration was used just about as economically as that of the ordinary ration, when the men were doing hard muscular work, implies, though it does not prove, that the energy of alcohol was used like that of carbohydrates for heat or muscular work or both. The results are not absolutely decisive, but the balance of probability seems to me to strongly support the view that alcohol was in

these experiments a source of muscular energy, and that when taken in small quantities it may very commonly have the same action.

In speaking of alcohol as a source of heat to the body, the distinction between body heat and body temperature was emphasized. Here again we should insist upon a distinction, namely, that between alcohol as a source of muscular energy and alcohol as a food for muscular work. However clearly it may be demonstrated that the potential energy of alcohol may be transformed into muscular energy, practical experience shows that alcohol is, under ordinary circumstances and for people in health, not a good kind of food for work. The reason is doubtless to be found in the distinction between the action of alcohol as a food and as a drug, between its direct action upon the muscles and its indirect action through the nervous system.

Locomotives which draw railway trains are provided with machinery by which the engineer can apply the power of the steam in the boiler to brakes which will retard or stop the train. The energy in either case comes from the coal, but the fact that the energy of the coal can be used to stop the train does not prove that it cannot be used to pull it. To be sure the case here is not exactly parallel with that of the alcohol acting upon muscles and also upon nerves. If we could imagine that, instead of putting all the coal into the furnace, part of it were to be put into the machinery where it would retard or stop the motion, the comparison might be less inaccurate. The muscular system is controlled by the nervous system. The very fact that alcohol affects the nervous system, though in ways not fully explained, may make it decidedly inferior, as food for muscular work, to other food which, supplying the same energy, would not interfere with nervous activity.

The effect, or effects of alcohol upon muscular activity and efficiency for muscular work are far from being settled. That excess is injurious no one doubts. The question here is as to small quantities. So far as I can judge from what I have read of the results of observations with considerable numbers of men, an alcohol ration, taken during the day's work, seems generally disadvantageous. The English hygienist, Parkes, whose experiments on this subject are often quoted, is inclined to think that alcohol is worse than useless if taken during the working

period of the day, but that small amounts may perhaps be useful at night after a hard day's work is done.

Athletes in training generally avoid alcohol in any considerable quantities. Some abjure it altogether. This was the case with Miller, the winner of a famous six-day bicycle race in Madison Square Garden, New York, in 1898, in which he rode from twenty to twenty-two hours a day and covered a distance of 2007 miles in a little less than six consecutive days. On the other hand, the diet prescribed for English students in training for boat-races commonly includes small quantities of beer or wine. A late study of the diet of Sandow, "the strong man" whose feats of muscular strength are so astounding, showed that he was in the habit of taking beer daily.

The difficulty with sweeping generalizations on either side of the question is in the facts on the other side which cannot justly be ignored.

Protection of body material by alcohol.

One use of the fuel ingredients of ordinary food, as sugar, starch, and fat, is to protect other material of the food and especially of the body from oxidation. The body must have material to burn. It is constantly consuming its own material and it is constantly replacing that material from the food. If the food supplies as much material as is needed and no more, the body maintains its store more or less nearly constant. If the food exceeds the need, the store tends to increase; if there is not enough, the body store is drawn upon. As a matter of fact, the body is constantly changing its store of protein, fat, and other substances, though the changes from day to day, under ordinary circumstances, are very small. The body materials most affected by these changes, or at least the ones to which the most interest attaches in our present discussion, are fat and protein.

Protection of body fat.

In some of our experiments, the food was more than sufficient to meet the demands of the body and the store of fat was increased. This increase was practically the same with the alcohol rations as with the ordinary rations. In a larger number the food supply was inadequate and the body lost fat,

but the losses were in general no larger with the alcohol than with the ordinary food. The results of our experiments coincide with those of inquiry elsewhere in implying that alcohol is able to protect body fat from consumption. In an examination of the results of such inquiry, nearly all of which has been conducted in Europe, I have found practically no case in which there is any adequate evidence to show that alcohol does not have such action, and, so far as I have observed, it is the belief of experimenters, generally, that alcohol does serve as a protector of body fat. Our experiments are the only ones in which the power of alcohol as compared with that of the fats and carbohydrates of ordinary food to protect body fat has been quantitatively measured. Comparing isodynamic amounts, *i. e.* the amounts that yield equal quantities of energy, the alcohol was very nearly as efficient as the fats or carbohydrates of the food which it replaced.

To put it in another way, an ounce of alcohol is isodynamic with three quarters of an ounce of fat or an ounce and three quarters of sugar or starch. The ounce of alcohol was nearly or quite as efficient as the isodynamic amounts of the other materials. I speak of this especial subject, however, with some reserve because, as I have already said, the experimental inquiry is not yet sufficient to tell us exactly how the different fuel ingredients of the food compare in efficiency in this respect.

Protection of body protein.

. One of the hardest fought questions in this whole discussion is whether alcohol does or does not act as a protector of body protein. The evidence is found in a large number of experiments with men and domestic animals, as dogs and sheep. Some of these seem to favor while others oppose the belief that alcohol has this action. Most of the earlier experiments, however, are lacking in the detail and accuracy needed to make them decisive. Of the later experiments, three series with men, namely, those of Miura, Schoeneseiffen, and Schmidt, have seemed to their authors and other students of the subject to imply that alcohol does not protect protein from consumption. Some have gone so far as to infer that its only action in this respect is to increase what we call proteid katabolism, that is, the breaking down of protein in the body.

This is an important matter. The essential tissues of the body consist largely of protein compounds or proteids, as they are otherwise called. The proteids are the basis of blood, and muscle, and bone, and brain. A substance which, instead of protecting these materials from consumption, tends to cause their dissolution, must be the opposite of food and the opposite of beneficial. Referring for details to what was said regarding this question in the previous chapters, the outcome may be briefly summarized. In the experiments of Miura, Schmidt, and Schoeneseiffen, as in most of those which preceded, the alcohol periods were short, not over six and generally not more than four days. In 1899 Neumann made experiments with longer alcohol periods, and found, during the earlier days, results like those of the three experimenters just named, but in the succeeding days, the body excreted no more nitrogen with the alcohol than with the ordinary diet; that is to say, the protein was apparently as well protected with the alcohol as with the nutrients which it replaced. He proposed the theory that alcohol may have two opposing tendencies, one by which it protects, and the other by which it tends to disintegrate protein. We might state it in another way, and say that the alcohol acts in the one case as a food, and in the other as a drug. The latter action would be that of Miura's proteid poison. Neumann suggested further that the body might become immune to this action, just as it acquires tolerance for other drugs. He would thus expect that the failure of alcohol to protect protein would be most apt to occur with people unaccustomed to its use, and would be temporary. This agrees with actual observation in a number of experiments.

Dr. Rosemann of the University of Greifswald in Germany, who had been for some time the leading exponent of the theory that alcohol does not protect protein, and is a proteid poison, and under whose direction the experiments of Schmidt and Schoeneseiffen were made, followed Neumann's publication with a number of articles in medical and other journals, in which Neumann's experiments and conclusions were subjected to keen and forceful criticism. He maintained that there were defects in both the planning and the interpretation of Neumann's work, and vigorously upheld the anti-protection and proteid-poison theory. Meanwhile other investigations were published by

Chotzen, with the coöperation of Rosenfeld and by Clopatt, which strongly sustained Neumann's view. Neumann, without replying to Rosemann, made further experiments which were so planned as to meet Rosemann's criticisms, and obtained results which strikingly confirmed his previous experiments and his interpretation of them. Finally Rosemann himself conducted two different series of experiments planned in accordance with the rigid canons of criticism which he had laid down. To his great surprise, as he tells us, he found indisputable evidence of protein protection by alcohol. In a critical and exhaustive review of the whole subject, lately published, Rosemann says that the protein protecting power of alcohol is established. He adopts Neumann's explanation of the conflicting results of previous experiments, namely, that alcohol may have, especially with persons but little accustomed to its use, a temporary tendency to increase proteid katabolism, but that the organism adapts itself in a short time to the alcohol, so that its disintegrating action ceases, and its nutritive action comes into full play.

In a lately published work, Rosenfeld discusses the various phases of the physiological action of alcohol with a keenness of insight and scholarly breadth of view seldom excelled. Like Rosemann he considers the protein protecting power of alcohol as established. As regards the disintegrating power, he is less certain.

Our own experiments, though not planned for the special study of this subject, throw some light upon it. The results agree with those of other experimenters in implying that alcohol sometimes protects protein, and sometimes fails to do so. They are not as conclusive, however, as the later experiments just described, mainly because the experimental periods were not long enough. When they were planned, we did not realize the importance of long periods which has since been made clear. If we had known it, we should hardly have been able to make such experiments with men in the respiration calorimeter; it would be a very tedious task for a man to remain in the chamber of the apparatus for twenty or thirty consecutive days and nights, and the cost of such inquiries would have been beyond our resources.

Conclusions. — Referring to the previous chapter for details

of the experimental evidence regarding the protecting and disintegrating action of alcohol upon proteids, the relative efficiency of carbohydrates, fats, and alcohol for proteid protection, and the sources of uncertainty and error in experimenting upon the subject, including the question as to how much of the katabolized proteid comes from organized tissue, the conclusions which seem warranted by the data now at hand may be summarized as follows:—

1. Alcohol may and does protect body protein.
2. Alcohol sometimes fails to protect protein. The designation of alcohol as a proteid poison is permissible as the expression of a plausible theory, but not justified as a statement of attested fact.
3. As regards efficiency for protecting protein, the carbohydrates, fats, and alcohol rank in the order named.

Availability and fuel value of alcohol.

Alcohol is similar to the fuel ingredients of ordinary food, the carbohydrates and fats, in that it is oxidized in the body, yields energy for warmth and probably for work, and protects body material from consumption. It thus serves the body as fuel. How does it compare with them in availability and fuel value? The word "availability," as here applied to the ordinary nutrients, expresses the proportion which is digested and made available for the building and repair of tissue and the yielding of energy. This proportion is the difference between the total amounts in the food and those excreted by the intestine. In like manner the available alcohol would be the difference between the total amount ingested and the amount excreted by the lungs, skin, and kidneys, practically none being excreted by the intestine. The available energy is the energy of the material actually oxidized, and is taken as the measure of the fuel value. The following table compares the coefficients of availability and the fuel values of the protein, fats, and carbohydrates of ordinary food as commonly eaten with the corresponding factor for alcohol as found in these experiments:—

Availability and fuel value of alcohol compared with those of nutrients of ordinary diet.

		Protein.	Fats.	Carbohydrates.	Alcohol.
Coefficients of availability	Materials, per cent. .	92	95	97	98
	Energy, per cent. . .	70	95	97	98
	Calories, per gram .	4.0	8.9	4.0	6.9
Fuel values	Calories, per pound .	1820	4040	1820	3130

The figures for coefficients of availability of materials mean that of every 100 parts by weight of protein in ordinary diet, 92 parts are digested, absorbed, and made available for building tissue and yielding energy. The corresponding factors for fats and carbohydrates are larger, 95 and 97 per cent. respectively, while the coefficient for alcohol, 98 per cent., makes it the most completely available of all. The coefficient of availability of energy of protein is only 70 per cent., as compared with 90 per cent. for the availability of the protein itself as material for use in the body. The reason for this difference is that the available protein is not completely oxidized, part of it leaving the body in urea and other compounds which still contain potential energy. This energy is estimated to average 22 per cent. of the whole; adding it to the 8 per cent. in the unoxidized protein of the feces, the sum, 30 per cent., represents the unused energy, and consequently the available energy is 70 per cent. of the whole. With the fats, carbohydrates, and alcohol, the coefficients for available energy and available material are the same, because the available materials are completely oxidized in the body. A gram of protein, as actually broken up and oxidized in the body, is estimated to yield 4 calories of energy as heat or heat and external muscular work. This is taken as the measure of the fuel value, and corresponds to 1820 calories per pound. In like manner a gram of fat would yield 8.9 and a gram of alcohol 6.9 calories.

Isodynamic quantities are those with like fuel values. Taking the fuel values of the substances as stated in the table, a simple calculation shows that 1 gram of alcohol would yield the same energy as 0.78 gram of fat or 1.73 grams of protein or carbohydrates. Roughly speaking, 4 grams of alcohol are iso-

dynamic with 7 grams of sugar, starch, or protein and with 3 grams of fat.

Further considerations regarding the action of alcohol.

The above view of the fuel value of alcohol considers only its action as food, and leaves out of account its action as drug. This distinction cannot be emphasized too strongly in such a discussion as the present. It is brought out very plainly in the following statement by Sir Michael Foster, the eminent English physiologist : —

“The value of the various articles of diet does not depend by any means solely on their ability to supply energy ; we have seen, for instance, that salts, which supply no energy, are nevertheless of use in directing the changes going on in the body. In a somewhat similar way, alcohol and other substances may influence and direct these changes. Whether that influence is beneficial or not will depend upon many circumstances, and certainly upon the quantity taken. We have many illustrations that a substance taken into the body in a certain quantity will produce one effect, and in another quantity it may have quite an opposite effect. There is no doubt that a certain quantity of alcohol is injurious and interferes with all the functions, and ultimately brings about various diseases, but it does not follow from this that, in a smaller quantity, it may not be harmless and even beneficial.

“Alcohol produces its most marked effects on the vascular and nervous systems. It leads to a dilation of the small blood vessels of the skin, and so to a larger flow of blood to the surface of the body ; this, while it produces a sensation of warmth, leads to an increased loss of heat by radiation and perspiration. If the amount of alcohol taken is excessive, the loss of heat will lead to a definite fall of temperature. Alcohol is then of no service as a preventive against cold. . . .

“The limit up to which any beneficial effects are produced by alcohol is soon reached, and beyond that it only does harm. This limit is not the same for all individuals ; a quantity good for one may be injurious for another, and a large number of people find that strictly moderate quantities of alcoholic beverages do them no harm, while others find that similar amounts impede them in their daily work.” (Foster and Shore’s “Physiology,” p. 156.)

Alcohol and the mental functions.

Of the effects of alcohol upon intellectual activity and efficiency, this is hardly the place to speak, as the subject has been well discussed by Professor Abel in the present volume. I venture, however, to quote the following statement, which summarizes, as well as any such brief statement can, the views which, so far as I have learned from reading and personal conversation, are held by the investigators whose judgment is most accepted by their fellow-specialists:—

“A small amount of alcohol may promote the action of the central nervous system, and often appears to quicken the rapidity of thought and to excite the imagination, but more usually, and always when taken in any but small quantities, it diminishes the power of connected thought and judgment. It also diminishes the power of receiving sensory impressions, and at the same time blunts all the special senses. Since it reduces the sensibility to cold and fatigue, and allays mental pain and worry, it is often resorted to and then with great danger.” (Foster and Shore’s “Physiology,” p. 157.)

Current errors regarding the nutritive value of alcohol.

The theories that alcohol is not oxidized in the body; that it is oxidized too rapidly to be of service; that it interferes with normal oxidation of food and body material; that when it is oxidized, the energy thus liberated is wasted by the increase of heat radiation from the body; that it does not supply the body with heat; that it is not a source of muscular energy; that it does not protect body fat and protein,—were all suggested by experimental facts. They have all been maintained by physiologists in good standing, and most of them are still found in reputable treatises. They are all used as staples of current temperance teaching. In the light of the present experimental evidence, neither is established, most are disproved, and no one is decidedly probable.

I venture to suggest that in the action of alcohol as drug there is enough of established fact to condemn not only its excessive use, but also its general use by people in health, without having recourse to theories regarding its nutritive value which cannot stand searching criticism.

Alcohol compared with ordinary food.

In its nutritive and other effects alcohol resembles and differs in a variety of ways from ordinary food materials and their nutritive ingredients.

Food vs. drug. — The chief effect of food is nutritive, while the most important action of alcohol is pharmacodynamic. This distinction between alcohol as food and as drug is fundamental.

Quantity. — The effect of both ordinary food and alcohol varies with the quantity. But the change with changing quantity is much greater with alcohol. Both are injurious when taken in excess, but excess of alcohol is injurious in more ways and in a greater degree. This is because of its action as drug, which may be hardly noticeable with small, but is deleterious and often disastrous in large quantities.

Moderation vs. excess. — Many physicians and hygienists believe that one-sided and excessive diet does more harm to the health of the community as a whole than the misuse of alcohol; that in this respect the "eating habit" is worse than the "drinking habit." But, however true this may be, it is to be remembered that all eat daily, while there are many who drink little or not at all, and that the injury to health from alcoholic excess, when it does occur, is more intense and destructive.

Tendency to excess. — Still more serious is the tendency of moderate drinking to lead to excess; the craving for alcohol is apt to come with the using, and sadly often it grows upon the user until he is powerless to resist.

Saddest of all is the effect upon the mental functions, the weakening of the will and the deadening of the moral sensibilities, the ruin of character which is wrought by alcohol as drug. It is only when alcohol is taken in moderate quantities that its action as food is of consequence. Roughly speaking, a "moderate" quantity in a given case might be the amount which could be taken without any manifest effect upon the nervous system. Just what quantities are moderate will depend upon the individual, the kind of alcoholic liquor, and the time and way it is taken. Thus persons accustomed to alcoholic beverages can tolerate more than those who are not. When the alcohol is diluted, as in wine and beer, it is less intoxicating

than when it is taken in more concentrated form, as brandy or whiskey with only a little water. So likewise more is tolerated with a meal than on an empty stomach.

The only test of what may be considered a moderate quantity, then, in this sense, is actual experience, and this is often a very unreliable criterion, when it depends upon the judgment of the user. While any quantity of alcohol too small to sensibly affect the nervous system may have a nutritive action proportioned to its fuel value, this would by no means decide its actual usefulness or desirability. A much smaller quantity taken habitually might prove disastrous, and then could hardly be called moderate.

Alcohol and digestion. — Before ordinary food can become available for the nourishment of the body, it must be digested. Alcohol is predigested food. Food is digested by processes of fermentation. Alcohol is a fermented product.

Different food materials have more or less influence upon the secretion of the digestive juices or upon the peristaltic action of the intestine, and hence upon their own digestion and that of other food. Alcohol in moderate quantities may and at times does stimulate the secretion of the digestive juices. It may also impede their action after they are secreted. It thus aids or hinders digestion. Under just what circumstances it helps or hinders is not yet fully understood.

Nutritive values. — To make the discussion of nutritive values clear and accurate, we must compare alcohol not simply with food in general, nor even with particular food materials, as bread or meat, but with the nutritive ingredients, or nutrients as they are often called, of which ordinary food consists.

We have here to do mainly with : —

1. Protein compounds, of which the most important are the proteids, such as myosin of lean meat, albumin (white) of egg, casein (curd) of milk, and gluten of wheat.¹ These are characterized by containing nitrogen.

¹ Much confusion results from the wide difference of usage with respect to the terms applied to these compounds. The usage here followed is that adopted provisionally by the Association of American Agricultural Colleges and Experiment Stations. It makes protein (as determined by multiplying nitrogen by 6.25 or other factor) a generic term to include both the proteid and non-proteid nitrogenous compounds. See page 194 above.

2. Fats, such as the fats of meat, and milk (butter), and oil of corn, wheat, and olive, etc.

3. Carbohydrates: the sugars and starches, including glycogen.

4. Mineral matters, as phosphates, sulphates, chlorides, and other compounds of potassium, calcium, and iron.

Water is essential for nutrition, but not commonly classed as a nutrient.

Functions of nutrients and alcohol. — The two chief functions of food are the building and repair of tissue and service as fuel; though other uses, as those of the mineral salts in regulating metabolic processes, are equally necessary to the support of life.

The protein compounds of food are the chief tissue formers. They also yield energy by their cleavage and oxidation, and thus serve as fuel. By their cleavage carbohydrates and fats are formed. One of their most important functions is to serve as the basis of protoplasm; in so doing they are believed to exercise great influence upon the metabolism of other substances.

The fats of food are transformed into body fat, and stored as such for future use. Their chief service is as fuel, and is rendered by their oxidation either without or after being so stored in the body.

The carbohydrates of food are to some extent transformed into fat in the body, and thus stored for future use. Their chief service is as fuel, and is rendered by their oxidation.

Alcohol is oxidized in the body, and thus serves as fuel.

All of the ordinary nutrients in serving as fuel protect one another and body material from consumption. Alcohol protects protein and fats from consumption, and there is every reason to believe that it protects carbohydrates also.

Oxidation and storage. — Alcohol resembles ordinary foods in being oxidized in the body. It differs from them in that it is not held by the body for any considerable time for future use.

Service as building material and as fuel. — Considering the body as a machine, the proteids supply material for building and repair. When they are broken down and oxidized, they yield energy and thus serve also as fuel; the bulk of the fuel,

however, consists of carbohydrates and fats. The fats, carbohydrates, and alcohol differ from protein in that they cannot build or repair (nitrogenous) tissue. All four are alike in that they are oxidized and yield energy, but the carbohydrates and fats are the fuel materials *par excellence*. Alcohol considered as fuel may be compared with the fats and carbohydrates. For this comparison it is necessary to distinguish between the ways in which the service as fuel is rendered.

Forms of energy. — All three classes of nutrients and alcohol likewise contain potential energy which becomes active when they are broken up and oxidized in the body. The energy thus liberated takes the forms of heat and muscular power. It may be that mental and nervous activity consist in transformations of physical energy, but this is a still unsettled problem. Heat, electrical energy, and mechanical energy are the only forms definitely known in the body, and of these heat and mechanical energy are the only ones of general importance, so far as their external manifestations are concerned. They are the only forms of energy commonly measured in nutrition experiments.

The fuel value of food or of a given nutrient is measured by the energy which can be made active by its cleavage and oxidation in the body. The fuel values are estimated in calories, as stated on p. 280.

The service of food as fuel is rendered in several ways: —

1. Food is oxidized and its latent energy is made available. About 70 per cent. of the energy of the protein, 95 per cent. of that of the fat, and 97 per cent. of that of the carbohydrates of ordinary diet are thus placed at the disposal of the body. When alcohol is taken in moderate quantities, about 98 per cent. of the energy is made available.

2. The energy of food is transformed into heat which warms the body. All the available energy of the ordinary nutrients, protein, fats, carbohydrates, and all of that of alcohol is transformed into heat or into heat and external muscular work in the body. The values of the ordinary nutrients and of alcohol in moderate quantities for supplying the body with heat are directly proportional to their available energy.

3. The energy of food is transformed in part into muscular work. This is the case with all the ordinary nutrients, and is probably, if not certainly, the case with alcohol. How much of

the available energy of each class of nutrients or of alcohol is capable of being so utilized is not yet determined by experiment. The practical value of alcohol as part of a ration for manual labor is small, because of its action as drug.

4. By the oxidation of food and the liberation of its energy for use by the body other food and body material is protected from oxidation. The exact order of efficiency of fats, carbohydrates, and alcohol, for protecting body material, is not definitively settled. The best experimental evidence now at hand, however, implies that their values for protecting fat are nearly proportional to their available energy, that is to say, a calorie from one appears to be as effective as a calorie from either of the others. For protecting body protein the same kind of evidence implies that calorie for calorie, the carbohydrates are the most and alcohol the least effective, the fats coming between the two, but perhaps nearer alcohol.

Is alcohol food? — The answer to the question depends upon the definition of food.

Of the two chief functions of food, (1) building or repair of tissue, and (2) service as fuel, alcohol performs only the latter. It is not food in the sense that bread and meat are food. It cannot be taken in large quantities by ordinary people in health without intoxication, and even if large quantities are tolerated it cannot support life permanently; it lacks the nitrogenous and mineral constituents which the body requires for tissue building and numerous other purposes. In certain forms of disease people often take quantities of alcohol which would be powerfully intoxicating if they were well, but in their illness the alcohol, instead of causing intoxication, helps them through a time of stress when they could not well tolerate ordinary food. Old toppers often drink large quantities of alcohol and eat little ordinary food. In these cases alcohol seems to act as food.

Besides power to build tissue and yield energy several other qualities are necessary or desirable in food.

Food should be palatable or capable of being made so by cooking or otherwise. To some people alcohol is palatable, to others it is not, but the taste for it is easily acquired.

Food should be digestible, *i. e.* capable of being changed so as to be absorbed from the alimentary canal. Alcohol is readily absorbed without change.

Food should "agree" with the eater. Some people cannot take milk without discomfort, others are made ill by eggs, and others by strawberries. It seems to be literally true that "one man's meat is another man's poison." In this sense alcohol in small quantities "agrees" with many if not most people; but in large quantities it is poisonous, and in large enough doses it is fatal. Smaller quantities taken habitually may cause disease and even death.

Moderate quantities of ordinary food are healthful and absolutely necessary, but excess is injurious. Whether alcohol in moderate quantities is harmful or not, it certainly is not necessary to people in health, and excess of alcohol is worse than excess of ordinary food. The evil of alcohol is increased by the tendency to excess, nor is it easy to say how small the quantity must be in order to be innocuous. People are sadly apt to overestimate the amount of alcohol they can use without harm. The harm often comes before they know it, and when they find it out it is often too late to stop.

Considered as food alcohol is very expensive; a given number of calories of energy costs several times as much in alcohol as in sugar or starch or fat of ordinary food.

If we define food as that which, taken into the body, either builds tissue or yields energy, alcohol is food, but it is a very one-sided food.

If we confine the word food to materials which, like bread and meat, contain protein and build nitrogenous tissue, alcohol is not food; neither is starch, which is the chief constituent of such food materials as wheat, corn, rice, and potatoes, and makes up the larger part of the food of man.

If we exclude from the list of foods those things which are either injurious to health or tend to become so, we must exclude alcohol, in excess, but we must do the same thing with meat. Only it takes much more meat to constitute excess, and the tendency to excess is not so great as with alcohol.

If we consider in the list of foods all substances which may serve the body for nutriment, and which may be thus utilized in considerable quantities without sensible disturbances of normal bodily functions, alcohol must be included. This is the case in health, and is especially so in some forms of disease. But even when it causes no symptom of intoxication, its action

as drug may impair the efficiency for the most productive muscular or mental work.

Of the action of alcohol as drug and its use as medicine, this is not the place to speak. There is, however, one form of action for which it is highly prized by many persons in health. I refer to its exhilarating effect. This is manifested in the sense of relief from fatigue which alcohol sometimes brings after hard work, in its influence upon the emotions which tends to "good feeling," and by which it "gladdens the heart of man," and in the sympathy and help to social intercourse which the "social glass" affords. How much alcoholic beverages are really worth for these purposes, and whether, in a given case, the advantage counterbalances the danger of excess, are questions not to be answered by hard and fast rules.

The preponderance of evil resulting from the excessive use of alcohol has led many people to the belief that the only proper line of conduct is to avoid the use of alcohol entirely unless it be as medicine. It has also led them to feel any statement regarding the moderate use of alcohol, other than absolute disapproval, as injurious to the temperance cause, and hence reprehensible. If I may be permitted the expression of a personal opinion it is that people in health, and especially young people, act most wisely in abstaining from alcoholic beverages, but I cannot believe that the cause of temperance in general, or the welfare of the individual, is promoted by basing the physiological argument against the use of alcohol on anything more or less than attested fact.

CHAPTER V.

ALCOHOLIC BEVERAGES AND THEIR NUTRITIVE VALUES.

THE number of different kinds of alcoholic drinks used in different parts of the world is very large. The differences are due to the materials from which they are made and the methods of preparation. The characteristic ingredient of all is ethyl alcohol, produced by the fermentation of starch or sugar.

Alcoholic beverages are commonly divided into three classes: (1) wines, (2) malt liquors, and (3) distilled liquors. Other and less important classes are: (4) root beer and like beverages containing small quantities of alcohol, (5) koumiss and other preparations made from milk by the fermentation of the milk sugar, and finally, (6) alcoholic preparations sold as medicines under such names as bitters, sarsaparilla, celery compound, malt extract, and the like.

Alcohols.

Ordinary alcohol or so-called ethyl alcohol is one of a large number of organic compounds which are characterized by a group of atoms called hydroxyl. This group consists of one atom of oxygen and one atom of hydrogen, and is expressed by the formula OH. In the alcohols the hydroxyl group is united to another group containing carbon and hydrogen, called a hydrocarbon radical and varying in composition in the different alcohols. In methyl alcohol the radical is called methyl; it consists of one atom of carbon united with three of hydrogen, and is indicated by the formula CH_3 . Methyl alcohol, accordingly, has the formula $\text{CH}_3.\text{OH}$ or CH_4O . In ordinary alcohol the characteristic radical is ethyl, which consists of two atoms of carbon and five of hydrogen, its formula being C_2H_5 . The formula of ethyl alcohol is accordingly $\text{C}_2\text{H}_5.\text{OH}$ or $\text{C}_2\text{H}_6\text{O}$. Methyl and ethyl alcohols are the first two members of a series, each of which differs from the previous one by one atom of

carbon and two of hydrogen. Over 20 members of this series are known to chemists. Among the more common ones are the following : —

Name.	Formula.	Boiling Point.	
		Centigrade.	Fahrenheit.
Methyl alcohol . . .	$\text{CH}_3.\text{OH}$ or CH_4O	66°	151°
Ethyl alcohol . . .	$\text{C}_2\text{H}_5.\text{OH}$ or $\text{C}_2\text{H}_6\text{O}$	78°	173°
Propyl alcohol . . .	$\text{C}_3\text{H}_7.\text{OH}$ or $\text{C}_3\text{H}_8\text{O}$	97°	207°
Butyl alcohol . . .	$\text{C}_4\text{H}_9.\text{OH}$ or $\text{C}_4\text{H}_{10}\text{O}$	117°	243°
Amyl alcohol . . .	$\text{C}_5\text{H}_{11}.\text{OH}$ or $\text{C}_5\text{H}_{12}\text{O}$	131°	268°
Hexyl alcohol . . .	$\text{C}_6\text{H}_{13}.\text{OH}$ or $\text{C}_6\text{H}_{14}\text{O}$	157°	315°

Methyl alcohol is commonly obtained by the destructive distillation of wood, that is, by heating wood without the access of air. Hence the familiar name of wood alcohol or wood spirit. It is a light, colorless, and very inflammable liquid.

Ethyl alcohol, or ordinary alcohol, is the most common of the alcohols, and when alcohol is spoken of without qualification, ethyl alcohol is ordinarily meant. It is formed in large quantities by the fermentation of vegetable products containing starches and sugars. It was originally obtained from wine, hence the name "spirits of wine." Pure ethyl alcohol, otherwise called absolute alcohol, is a colorless, volatile, inflammable liquid, lighter than water; its specific gravity is 0.79, that of water being 1.

Propyl, butyl, amyl, and hexyl alcohols are also formed in fermentation. Like methyl and ethyl alcohols, they are colorless and inflammable. They occur in fusel oil, of which amyl alcohol is the chief constituent.

Besides the alcohols of this series, many others are known to chemists. Thus glycerin is an alcohol, formed by the union of the radical glyceryl, C_3H_5 , with three equivalents of hydroxyl, so that its formula is $\text{C}_3\text{H}_5(\text{OH})_3$ or $\text{C}_3\text{H}_8\text{O}_3$.

The characteristic alcohol of ordinary liquors is ethyl alcohol. Distilled spirits generally, and beer and wine as well, contain more or less of other alcohols, especially amyl alcohol and small quantities of glycerin, together with organic acids, esters, and other products of fermentation.

Fermentation and ferments.

When the juice of grapes or other fruit is allowed to stand, bubbles of carbonic acid gas appear, and at the same time alcohol is formed. The same thing takes place if yeast is added to a solution of sugar. To this process, by which sugars and starches are changed to alcohol and carbonic acid, the term fermentation was originally applied. To many persons this term always suggests a chemical process in which gas is developed, but the word fermentation has come to have a much wider signification.

The processes of fermentation are due to the action of substances which are called ferments, and are commonly divided into organized and unorganized ferments. The unorganized ferments, or enzymes, are substances which have no organized structure, although they are produced by living organisms. Familiar examples of enzymes are the digestive ferments, as ptyalin of the saliva, pepsin of the gastric juice, and trypsin and steapsin of the pancreatic juice. Diastase of malt, which converts starch into dextrine and sugars, is another familiar enzyme.

Organized ferments, as the name implies, have an organized structure, so that they live, grow, and multiply, and their growth under suitable conditions is accompanied by various forms of fermentation, of which that caused by yeast is an example. The natural fermentation by which wine and cider are produced is caused by organisms which gather from the air upon the fruit. The secondary fermentation by which the alcohol of wine and cider is changed to the acetic acid of vinegar, and the conversion of milk sugar to lactic acid by which the milk is made sour, are further examples of the action of organized ferments.

A large number of kinds of organized ferments are included under the designation bacteria, while others are called yeasts. Various kinds of disease are also caused by bacteria, though in some cases the immediate cause of the disease seems to be found in products of the fermentation which they induce. Some of these products are poisonous, though it does not necessarily follow that a substance is poisonous because it is produced by fermentation. Indeed, various kinds of fermentation are essential to life, as is the case in digestion.

The enzymes are produced by living organisms. Thus pepsin

is produced by the peptic glands of the stomach. Enzymes can be extracted from bacteria which will cause the same fermentations as the bacteria themselves, and the same is true of the enzymes of yeast. Within a few years means have been found to extract even the alcoholic ferment from yeast. It is coming to be believed that the action of the organized ferments is due to the characteristic enzymes produced by them.

Alcoholic fermentation.

The fermentation by which alcohol is produced is chiefly brought about by the yeast plant, *Saccharomyces cerevisiae* (brewers' or bakers' yeast), growing in the presence of sugars or starchy materials, although numerous other yeasts and certain species of bacteria are capable of producing alcohol. Indeed, alcoholic fermentation appears to be an extremely common process, and there are reasons for believing that alcohol is produced very generally but in small quantities by the natural fermentation of vegetable matter.

For instance, Müntz¹ reports the discovery of alcohol in cultivated soil, rain-water, sea and river water, and in the atmosphere. It is to be noted that the presence of alcohol was shown by the iodoform test, and that this test is also given by a number of compounds² as acetic ether, aldehyde, levulimic acid, etc., so that the actual occurrence of alcohol in these cases, though probable, is not absolutely proven.

More recently Godlewski and Polzeuiusz³ have performed experiments which led them to believe that alcohol is produced during the intramolecular respiration of seeds in water, and to think it probable that in all cases where the respiration takes place at the expense of carbohydrates, the chemical action is practically identical with ordinary alcoholic fermentation.

The belief is also more or less common that alcohol may be produced in the human body as the result of the intestinal fermentation of carbohydrates under the influence of the *Bacillus coli communis*. Harden⁴ in 1901 reported the results of an

¹ *Pop. Sci. Monthly*, xix. (1881) 238 ; translated from *La Nature*.

² See Liebens, *Ann. der Chemie*, Sup. Bd. viii. 218.

³ *Bull. Acad. Sci.*, Cracow, 1901, 227 ; Abst. in *J. Chem. Soc.* 80, ii. 618.

⁴ Harden, "The chemical action of *bacillus coli communis* on carbohydrates," *Trans. Chem. Soc.* lxxix. 610.

investigation upon the action of this bacillus and similar organisms on carbohydrates and allied compounds. He found that in the fermentation produced by the growth of these bacteria, the glucose is converted into formic, acetic, lactic, and succinic acids, carbon dioxide and hydrogen, and that ethyl alcohol was also produced in amounts varying from 9 to 17 per cent. of the weight of glucose fermented. All the products were estimated quantitatively and by approved methods. The alcohol was estimated by acidifying the solution with oxalic acid, and distilling; the distillate was then exactly neutralized and again distilled through a fractionating column, the distillate collected, and the alcohol calculated from the specific gravity.

Since the *Bacillus coli communis* is normally present in the intestine, it is not unnatural to assume that the same action takes place there.

Production of alcoholic beverages.

It thus appears that alcohol is produced mainly from sugars and starches. The sugars which can undergo alcoholic fermentation without previous change are mainly the glucoses, especially dextrose and levulose, which occur ready formed in the juices of fruits. Cane sugar and milk sugar are converted into glucoses; starches and similar substances are broken up into simpler compounds like dextrin and maltose and then into glucose by diastatic ferments before the alcoholic ferments can decompose them.

The occurrence of ready-formed glucoses in fruits helps to explain why their juices undergo alcoholic fermentation so readily, — in other words, why wine and cider are produced when the juices are acted upon only by ferments from the air: they ferment naturally.

To obtain alcohol from the starch of cereals, grains, potatoes, and the like, it is first changed to dextrin and glucose, generally by the aid of diastatic ferments. For this malt is used. In making malt, grain, generally barley, is moistened and kept in a warm place until it "sprouts," *i. e.* germinates. Diastase is thus developed and begins the change of the starch of the barley to dextrin and sugar. When this process of malting has gone far enough, the malt is dried and ground, put in water, and kept in a favorable temperature for the further development and action of the diastase.

If malt liquor is to be made, ground grain or sugar is added to supply more material to be fermented. Hops are put in for the sake of their bitter principle, or other bitter substance is used to secure the desired bitter flavor. Yeast is added to the wort, as it is called, and increases the diastatic and causes the alcoholic fermentation. The treatment depends upon the kind of liquor to be produced, whether beer, ale, or porter. Which-ever is made, it consists of the liquid which is drawn off and stored for use. It contains considerable dextrin with a little sugar; ethyl alcohol and more or less of other alcohols including glycerin; lupulin; carbonic, acetic, lactic, and succinic acids, and mineral salts.

For making such distilled liquors as whiskey, gin, or schnapps, the starch is obtained either from some kind of grain, as rye, maize, or oats, or from potatoes or sugar beet pulp. The material is ground and mixed with water and made into a mash with malt. Yeast is added and the fermentation kept up until as much as possible of the starch and sugar are fermented to alcohol. The products of fermentation are nearly the same as in the wort made for beer. The liquid is drawn off and distilled. The alcohol is more volatile than the water, so that when the liquid is heated in the distillation, the alcohol passes off first, though it carries with it more or less of the water and other volatile products, including fusel oil and glycerin. By re-distillation or other process of rectification, the alcohol is obtained more or less nearly pure.

Rum is made by diluting molasses, which contains cane sugar and glucose, fermenting and distilling.

Wine is distilled in similar manner, yielding brandy which, properly rectified, yields more or less pure alcohol.

Materials other than alcohol in liquors.

Wine, malt liquors, and distilled liquors contain a variety of compounds other than water and alcohol. Some are contained in the fruits, grains, or other vegetable products from which they are made; some are formed in the fermentation, and some are added in the manufacture for flavoring, coloring, or preserving the liquors.

Compounds extracted from the fruit, grain, etc. — The must or unfermented juice of grapes, apples, and other fruits contains

proteid matters, sugars, gum, coloring matters, tannin, organic acids especially tartaric acid, also potassium tartrate and mineral salts. In making the wine, much if not most of the sugar is fermented and more or less of the proteids are removed. The greater part of the tartaric acid crystallizes out as argol or crude potassium bitartrate. The most of the other materials remain in the wine. In making malt liquors, the wort contains dextrin, proteids, and mineral salts, which are not removed in the fermentation but remain in the liquor. When the wort is prepared for distillation and distilled, the spirits contain very little of these substances.

Compounds produced by fermentation.—In the alcoholic fermentation of sugars, ethyl alcohol is the chief product, but propyl, butyl, and amyl alcohols, glycerins, various organic acids and esters (sometimes called compound ethers) are produced. These are formed in wines. The chief acids in wine, aside from tartaric, are acetic and succinic.

The characteristic acid of cider is malic, as that of wine is tartaric.

In the making of champagne and other sparkling wines, the later part of the fermentation takes place in the bottle, which is kept tightly closed so that the carbonic acid is retained until the bottle is opened, when it comes out with active effervescence.

The esters in wines are compounds of organic acids with the alcohols formed in the fermentation. Among them are ethyl acetate, pelargonate, and tartrate. They give the bouquet and much of the flavor to the wine, although their quantity is extremely small. They develop gradually sometimes through long periods of years. This helps to explain why old wine is so much superior to new in bouquet and flavor. The natural odors and flavors of fruits are due to these and similar compounds, and many of them are closely imitated by esters of chemical manufacture. The following are some of the natural odors and flavors and the corresponding compound ethers:—

Apple	Amyl valerate.
Jargonelle pear	Amyl acetate.
Quince	Ethyl pelargonate.
Pineapple	Ethyl butyrate.
Green gage	Ethyl cœnanthylate.
Wintergreen	Methyl salicylate.

A great variety of natural odors and flavors are imitated by mixtures of esters with each other and with other compounds known to the organic chemist. Such artificial products are sold in great quantities as fruit essences, and are used in flavoring alcoholic beverages.

Fusel oil.—In the fermentation by malt and yeast, lactic and succinic acids and propyl, butyl, amyl, and hexyl alcohols are formed. When the fermentation is carried as far as is done for the manufacture of spirits, the quantity of these may be considerable. Taken together, they make fusel oil, of which amyl alcohol is generally the chief constituent. Fusel oil is far more injurious to health than the same amount of ethyl alcohol. Though less volatile than ethyl alcohol, it is distilled off with the latter and remains in the spirits unless removed by careful rectifying. In the aging of spirits, as whiskey, it is partly changed to esters, with a more mellow flavor.

Materials added for flavor, color, and preservation.—The materials most used for actual betterment of wines are alcohol and sugar. In completely fermented wines, the glucose is almost wholly changed to alcohol. Hence Burgundy, claret, Rhine, and Moselle wines contain little or no sugar. Sweet wines, such as port, sherry, Marsala, Muscat, and some Tokays contain considerable unfermented sugar. A “dry” wine will contain less sugar than a “full bodied wine.” To prevent the sugar from further fermentation, sweet wines are fortified by addition of brandy. Cane sugar is added to champagne to give it body and prevent acetic fermentation.

When the juice of the grape, after pressing, is allowed to stand on the pressed residue or “marc” and ferment, it extracts coloring matter from the skins or “husks” and seeds. This gives the color to red wines. When the juice is separated from the marc as soon as it is pressed, white wine results.

Hops and other materials with bitter taste are used to flavor malt liquors as already stated. The color of beers, ales, and porter depends largely upon the malt. When the latter has been strongly heated, it imparts a dark color to the liquor.

In the preparation of brandy, whiskey, gin, cordials, and other spirits, a great variety of coloring and especially flavoring materials are used.

Genuine brandy, *i. e.* that made from wine and otherwise

called Cognac or French brandy, takes a yellowish color from the oak casks in which it is stored. It is sometimes colored more deeply by the addition of caramel (burnt sugar), which is used in coloring other liquors also. Much of the brandy of commerce, including so-called "British brandy," is made by flavoring "grain spirit" with esters, as acetate, nitrite, or pelargonate of ethyl; oils of cassia, cloves, and bitter almonds; tinctures of allspice, galls, capsicum, oak bark, etc.; and coloring with caramel and other material. Cognac is also imitated by distilling alcohol (proof spirit) with argol, bruised prunes, and a little Cognac, coloring with caramel and flavoring with tannin.

Gin is made by treating alcohol from grain with flavoring material and re-distilling. The materials used for flavoring gin are numerous and include juniper berries, oil of juniper, turpentine, almond cake, coriander seeds, capsicum, orris, and angelica roots, etc., and sometimes sugar. So-called Hollands and (Dutch) Schnapps are similar to gin.

Genuine rum, made by fermenting molasses and other residual products from the manufacture of sugar and distilling, is said to owe its characteristic flavor to ethyl butyrate and formate produced in the fermentation. Factitious rums are manufactured from grain spirit by flavoring with such substances as butyric and acetic esters, butyric acid, which forms butyric esters with the ethyl of the alcohol, and various vegetable oils or essences. Rums are colored by burnt sugar or by long keeping in casks.

Whiskey is made by adding various materials to spirits distilled from grain or potatoes. Logwood, catechu, tea infusion, burnt sugar, etc., are sometimes used for coloring. Various oils, essences, and the like are employed as flavors.

Liqueurs and cordials are highly flavored preparations from brandy or grain spirit. They are generally but not always sweetened. They are often brightly colored with such coloring matter as turmeric or cochineal or coal tar dyes, some of which are injurious. Absinthe, benedictine bitter, curaçoa, maraschino, and Swedish punch are common examples. Sweetened gin might be called a cordial.

Absinthe is flavored with various volatile oils, as oil of cinnamon, cloves, peppermint, anise, and angelica. Its character-

istic constituent is oil of wormwood, *artemisia absinthum*; the especially injurious character of the liqueur is attributed to this oil. The green color of absinthe is due to chlorophyll of the juice of the spinach, nettles, parsley, or other plants used in the preparation. The white turbidity or milkiness produced in absinthe by diluting with water, is due to the oils. Some varieties of absinthe have little sugar.

Of the materials used with spirits in the common proprietary articles containing alcohol and sold as medicines,¹ but little is known to the public. Such names as "celery compound," "sarsaparilla," and "malt extract," indicate the constituents for which medicinal value is claimed.

Injurious ingredients of alcoholic beverages. Adulterations.

The chief injury to health wrought by alcoholic liquors is attributable to the action of ethyl alcohol when they are taken in excess.

Fusel oil. — Leaving ethyl alcohol out of account, the most generally injurious substance is commonly believed to be fusel oil. The quantities of fusel oil in wine and beer are very small. Grain or potato spirits, unless well rectified, may contain such quantities as are believed to be very injurious to health. On long standing, more or less of the fusel oil of spirituous liquors undergoes chemical changes by which esters of agreeable odor and flavor are formed.

Some years ago the question of fusel oil in distilled liquors was investigated by the German imperial board of health. The outcome was hardly such as to sustain the old view as to the extremely deleterious action of fusel oils in ordinary distilled liquors. Late experiments² by Sir Lauder Brunton and Dr. Tunnicliffe, in England, seem to imply that the presence of fusel oil in such quantities as usually occur in potable liquors is not a serious menace to public health, but that the greatest danger is from the danger of furfural and other similar aldehydes which are derived from the husk of the grain under the influence of heat and acids.

Furfural. — Furfuraldehyde, otherwise called furfural or

¹ See report on this subject by Dr. H. P. Bowditch, pp. 344-347.

² With dogs, cats, rabbits and men. *Lancet*, 1900, ii, 1643, and 1902, i, 1551.

furfurol, is a compound produced by the action of dilute acids upon the so-called pentosans, which occur in the husk of grain, in straw, wood, and other substances containing so-called woody fibre. The pentosans are similar to cellulose and starch in that they break up into simpler compounds. The celluloses and starches which occur in the interior of the grain thus break up into sugars which contain six atoms of carbon in the molecule and are called hexoses; these ferment in presence of yeast, yielding alcohol. The pentosans also break up, but yield compounds containing five atoms of carbon to the molecule, whence the names pentose and pentosan. These do not yield alcohol like the hexoses under the action of alcoholic ferments, but by proper treatment they are changed into furfural (from Latin *furfur*, bran). It is claimed that in the modern processes of manufacture of alcohol from grain, the grain is more completely disintegrated and the bran is more fully decomposed than formerly. The result is that more fermentable material is set free and the output is larger. This breaking up of the bran might naturally result in the production of furfural. It is urged that furfural is present to a greater or less extent in all whiskeys, but it is especially abundant in all those made by modern processes by which it is sought to obtain as much liquor as possible per bushel of grain. Accordingly, the superiority of the liquors of the olden times was due not so much to the fact that they were "aged" as because they contained less furfural. In Brunton and Tunnicliffe's experiments, the after effects of intoxication with ordinary spirits were compared with those of spirits from which the furfural had been removed. In the latter case, as soon as the animal was sober, it appeared to be in perfectly normal condition and showed none of the after effects which in the former case lasted for a considerable time. This would imply that the furfural was responsible for the especially injurious action of the liquor containing it.

This consideration may, perhaps, have a bearing upon the investigations referred to beyond in which the quantities of fusel oil in liquors sold in New York city and in Massachusetts were found to be small. In the accounts of these investigations no special tests for furfural were reported, as was natural, since such are not customary. The late investigations of Lauder Brunton and Tunnicliffe suggest that the furfural and like compounds

may have been actually present and in injurious amounts. If this view is correct, it may be that the cheap liquors commonly sold are, after all, especially injurious. In other words, what Lauder Brunton and Tunncliffe claim for furfural may be found to justify the common impression that the cheap whiskeys and other cheap liquors now common are more injurious than purer liquors because they contain more of furfural and like poisonous ingredients.

Adulterations. — Just what are adulterations in beverages or food is largely a matter of definition, nor are all materials used for adulteration harmful. One of the most common adulterants is water, added to increase the quantity. The caramel used for coloring, even the sugar added to liquors for flavor, might be called adulterants. The same is true of the long list of vegetable oils, essences, and bitters, which are used for flavoring. Many, if not most of them, are commonly used to flavor food, and are considered desirable rather than injurious. Few, except absinthe, are generally regarded as deleterious.

A number of more or less objectionable materials are, however, used for the coloring, flavoring, and preserving of wines, beers, and distilled liquors. The use of plaster (sulphate of lime) in the preparation of wines is not uncommon, and is thought by many to be injurious to the health of the consumer. Salicylic acid is said to be used as a preservative of beers.¹ Among the materials which may occur naturally in excess or be added artificially, and are to be considered as more or less injurious adulterants, are : —

In brandy : methyl and amyl alcohol and tannin in excess, salicylic acid, zinc, lead, copper, and hot principles, such as cayenne.

In whiskey : fusel oil and water in excess.

¹ Lately (1900–1901) large numbers of cases of arsenical poisoning in England have been traced to arsenic in certain beers. Investigation showed that in the manufacture of these beers, glucose was used which had been prepared with sulphuric acid, which in its turn was made from pyrites containing arsenic. The sulphuric acid had previously been made from sulphur and no trouble had been found with the glucose or the beer. The arsenic was, however, directly traced from the pyrites through the sulphuric acid and glucose to the beers, and large numbers of the specimens of the latter were found to contain arsenic. This poisoning of beer will doubtless prove decidedly exceptional.

In gin : alum, sulphuric acid, lead, zinc.

In beer : salicylic acid, essential oils, picric acid, various bitter principles, atropin, strychnin.

In wine : elderberry, whortleberry, hollyhock, logwood, cochineal, indigo, aniline colors, plaster.

It is to be observed, however, that while the chemist is advised to look for these and similar substances in the regular course of examination for adulterants, yet of those which do not occur naturally in the liquors, few are commonly found, and a number of the worst ones are almost never detected.

Manufacture of inferior products.

There is another form of what is sometimes called adulteration which is very common, namely, the manufacture of inferior imitations. Such, for instance, are the wines which are made, at least, in part, from dried raisins or from the marc of grapes with the addition of distilled spirits and flavoring matters. The objection to such products is not that they are more injurious than the genuine articles, but that they are not what they are represented to be.

Inferior grades of distilled liquors. Cheap whiskeys. — There is a common impression that a large part of the injury to health which comes from the use of alcoholic beverages is due to deleterious ingredients, either fusel oil which has not been properly removed by rectification or substances which are added as direct adulterants. There is also a common impression that the cheap liquors contain large quantities of such harmful ingredients. That chemical analysis fails to confirm this view is shown by the results of official inquiries lately made in New York city and in Massachusetts.

In 1898 the New York Department of Health, through its chemist, Dr. Ernst J. Lederle, now Health Commissioner of New York city, tested the composition and quality of the cheap whiskey sold in that city. To this end samples of whiskey were collected in many saloons on the Bowery and neighboring streets of the East Side where it was sold at three cents per glass. They were bought by the pint at the usual retail prices, which varied from $17\frac{1}{2}$ to 40 cents, and averaged 23.8 cents. Two samples of "genuine whiskey," one old and the other new, were bought from a well-known and responsible firm for comparison. Dr.

Lederle's report of this inquiry has, so far as I am aware, not been published. From the manuscript he kindly permits me to quote the following:—

“Whiskey is an ardent spirit which is distilled from fermented grain, and is named from the particular grain used, as rye, corn, etc., each variety having its own peculiar flavor from the material used. The starch of the grain undergoes a process of fermentation, the products of which are ordinary, or ethyl alcohol, so-called fusel oil, organic acids, and other substances in small amounts. This liquid, when subjected to distillation, produces: water, alcohol, fusel oil, and volatile organic acids, and is quite, or nearly, colorless. The liquor is now subjected to a second distillation or to a purification process, the object being to reduce the fusel oil to a very small amount, and to remove certain objectionable impurities. This liquid should now contain from 50 to 60 per cent. of alcohol by volume, or if stronger, be reduced to that. This is new whiskey, having a somewhat rank, sharp taste and odor on account of the fusel oil it contains. To remove this and to generate the flavor or so-called ‘bouquet,’ the liquor is subjected to the ‘aging’ process, being stored in wooden casks for from two to six years or longer. The flavor has now changed, and the liquor is more mellow and peculiarly fragrant, the fusel oil having been, in part, converted into compound ethers. Extractive matter and tannin have been taken up from the wood, and the whiskey has acquired a brown color. This product is ‘straight whiskey.’

“From this straight whiskey is made the so-called ‘blended’ whiskey by mixing it with varying proportions of pure or ‘cologne’ spirit, proof, that is, having 50 per cent. by volume of alcohol.

“This cologne spirit is now made principally from the distillation of fermented corn, and on account of the improved methods of manufacture, the use of steam stills, etc., is made of great purity, consisting of alcohol and water without flavor or color.

“The high price of the well-matured (genuine) whiskey (there is an actual loss in volume of 20 per cent. in four or five years) has led to the compounding of a drink in imitation of whiskey, and this cheap article is made and consumed in large quantities.

"To prepare this 'artificial' or 'sham' whiskey, cologne spirit of proof or nearly proof strength . . . is colored with caramel, a harmless coloring matter made from sugar, and a sufficient amount of so-called whiskey oil or essence to produce the desired flavor. Sometimes a little prune juice, sugar, or glycerine are added to improve the taste.

"The whiskey oils consist either of a small amount of fusel oil mixed with compound ethers, or of the ethers only. Essences are the alcoholic solutions of the oils. These compounds represent very closely the ingredients existing in genuine whiskey, and when used in the proportions as directed, are harmless. One sample of 'essence of rye whiskey' examined contained acetic ether, acetic aldehyde, amyl alcohol, and it was calculated that when added to the spirit in the amount as directed, would not add quite 0.01 per cent. of fusel oil to the mixture, an amount which can be barely determined by our most refined chemical methods, and which amount is harmless."

The main results of the analyses, which are given in detail, are summarized in Table 7:—

TABLE 7. — *Analyses of samples of whiskey sold at 3 cents per (ounce) drink in New York City, 1898, as compared with "genuine" whiskeys.*

Kinds of whiskey.	Price per pint.	Specific gravity at 60° F.	Absolute alcohol by weight.	Absolute alcohol by volume.	Fusel oil by volume.	Total solids.	Ash.
"Genuine."	cents.		per ct.	per ct.	per ct.	per ct.	per ct.
"Old"	75	0.930	44.50	52.15	0.19	0.70	0.029
New	37½	0.938	40.92	48.37	0.35	0.18	0.012
Cheap grades.							
20 samples { minimum	17½	0.934	25.38	30.82	Trace ¹	0.07	0.002
{ maximum	40	0.967	43.24	50.82	0.19	1.32	0.026
{ average	23.8	0.950	34.74	41.47	0.06	0.35	0.010

¹ Trace = not over 0.01 per cent.

For the amount of alcohol in whiskey the standard of the U. S. Pharmacopœia is 40–44 per cent. by weight. The two samples of genuine whiskey came up to this standard. The cheap whiskeys ranged from 25.4 to 43.2, and averaged 35 per cent., five sixths of the standard.

The most objectionable ingredient, according to the report, was fusel oil. For the amount of this allowable in liquors,

there is no generally accepted standard, though it is often recommended that "not more than a trace" be present. The report considers from 0.20 to 0.25 per cent. by volume (0.17 to 0.20 by weight) the maximum that should be present in good liquors. This is considerably more than would naturally be called a trace. Of the samples examined, that of "genuine new" whiskey contained 0.35 per cent. This, however, it was understood was "not sold for general use, but intended for blending purposes." The sample of "genuine old" whiskey contained 0.19 per cent. Of the twenty samples of cheap whiskey, nine contained "a trace" (less than 0.01 per cent.); six had 0.10 or less and five between 0.10 and 0.19 per cent. by volume.

Tests failed to reveal any poisonous or injurious metals as antimony, arsenic, tin, lead, mercury, copper, and zinc; or mineral acids, or undue amounts of tannin, or injurious coloring matters. While "it was evident that in a number of samples, flavors were present, such as peppermint, prune juice, vanilla, cinnamon, bergamot, etc., foreign to genuine whiskey, the additions were harmless ones. In no case were capsicum (pepper), mineral acids, or other injurious substances, supposed to be used, found."

The report draws the following conclusions regarding the character of the cheap whiskeys:—

"Of twenty samples of whiskey purchased at places where it is sold at three cents per drink (of one ounce) almost all appear to be artificial or made up whiskey, compounded from spirits, caramel color, and flavoring essences.

"In no case was the amount of fusel oil present excessive.

"No injurious ingredients were found in any of the samples.

"An artificial whiskey, made from pure cologne spirits, about proof (containing about 50 per cent. by volume of alcohol), colored by caramel and flavored by a small amount of a non-injurious essence, is probably less injurious to the system than a genuine new whiskey, of the same alcoholic strength, containing 0.25 per cent. by volume or over of fusel oil."

The question as to whether it is possible to sell whiskey, free from deleterious ingredients, at three cents per drink, is answered by Dr. Lederle in substance as follows:—

The glasses in which the three-cent whiskey is dispensed hold just one ounce. Each gallon of liquor would thus give 128 drinks.

If those liquors were made from the very best spirits, either "cologne" spirit or ordinary alcohol, it was estimated that, taking into account the cost of materials, including colors and flavors, and also the amount of water added, they could be made for \$1 per gallon. At three cents per drink, 128 drinks would be sold for \$3.84.

The reader who is not a specialist might see in this report a tendency to judge the beverages rather leniently. Especially might it seem that the estimate of .25 per cent. of fusel oil as an allowable amount would be rather large enough, though it is no larger than is sometimes found even in high grade whiskeys. However, this may be, the examinations fail to give any evidence in favor of the belief that the cheap liquors are especially objectionable on account of their content of fusel oil or adulterants. Similar results were found in examinations of liquors sold in Massachusetts, as explained beyond.

It is to be especially noted, however, that neither the investigation by Dr. Lederle nor those by the Massachusetts Board of Health makes any reference to such compounds as furfural, to which attention has lately been called by Brunton and Tunnicliffe. (See pp. 325-327.)

General quality of liquors as commonly sold.

The Massachusetts Board of Health has reported two inquiries into the character of the alcoholic liquors commonly sold in that State, one with reference to pharmacopœial wines and liquors as sold by druggists, the other concerning the liquors sold in drinking saloons.

The results of the former are given in the Report of the Board for 1885-86, by the analyst, Dr. B. F. Davenport. In speaking of them the Secretary of the Board, Dr. S. W. Abbott, says:—

"Of the seventy-six samples of spirits obtained by the inspectors, nine only conformed to the requirements of the statutes, the departure from the standard being almost exclusively in the addition of water, alcohol, or of fruit sugars. The same was also true, in a still greater degree, of the 36 samples of wines, of which one only conformed to the strict requirement of the pharmacopœia.

"These examinations have also shown the falsity of a popular

impression, which has been created and fostered by the ill-advised statements of public lecturers, and also in published documents, that the harmful effect of the habitual use of alcoholic stimulants is due to the adulterations to which they are subjected, rather than to the alcohol which they contain. It is sufficient to say that such statements have no foundation in fact, nor are they in the interest of justice, temperance, or truth."

The results of the second inquiry are given in the Report of the Board for 1894, by the analyst, Dr. C. P. Worcester, who says:—

"An effort has been made to determine the quality of the liquor sold in the ordinary city saloon over the bar. To this end samples of whiskey, brandy, rum, gin, ale, beer, and cider, were collected, these samples being bought by the bottle or glass at various saloons, and paid for, thus representing what is actually sold every day to ordinary patrons. The analysis of these samples was made with the view of determining their relation to accepted liquor standards of strength, and also with a view of detecting any injurious ingredients or additions.

"There appears to be a popular idea that most saloon liquor is poisonous, and that most of the evil effects of intemperance are directly caused by the poor quality of the ordinary saloon stock. The conclusions to which this investigation has led, are, however, that the hard liquors usually differ from the standards chiefly in containing too much water or sugar, and that ingredients more injurious than alcohol are rarely to be found in appreciable amount. Fusel oil in noxious amount is occasionally to be found, and it is also rarely present to a distinctly appreciable extent in beer. It appears to be a common custom to preserve ale and beer by the addition of salicylic acid. The use of this drug for this purpose is everywhere recognized as harmful and unjustifiable."

The results of analyses of 175 samples of liquors are summarized in Table 8. The "standards" for percentages of alcohol accord with those of authoritative treatises, such as the U. S. Pharmacopœia.

TABLE 8. — *Analyses of liquors as sold over the bar in ordinary city saloons in Massachusetts.*

	Number of samples.	Alcohol in samples, proportions by weight.		Extract in samples. Average.
		Range.	Average.	
		Per cent.	Per cent.	Per cent.
Whiskey	37	30.7-46.0	37.4	.61
Brandy	37	21.3-50.7	40.5	.94
Rum	39	24.7-42.9	37.0	.51
Gin	34	29.5-42.5	38.1	—
Pale ale	7	3.5- 5.4	4.5	4.54
Beer	15	1.1- 7.1	4.5	5.93
Cider ¹	6	3.6- 8.0	5.7	4.19

“The ‘standards’ assumed were for alcohol in per cent. by weight: whiskey, 44 to 50; brandy, 39 to 47; rum, 42; gin, 40. Those for ‘extract’ were: whiskey, 0.25 per cent. or less, brandy, 1.5 or less.

“Of deleterious ingredients² other than alcohol there were reported:—

“*Whiskey*. — Excess of tannic acid in 5, tannic acid absent in 3 samples. Fusel oil present (‘in noxious amount’?) in one sample. Two samples were ‘chiefly brandy.’

“*Brandy*. — Excess of tannin in 4; acidity in excess in 3; fusel oil (in excessive amount?) in 2 samples; 2 samples largely or chiefly whiskey, and 2 chiefly alcohol and water.

“*Rum*. — 2 samples ‘new rum;’ 1 chiefly brandy; 2 practically alcohol and water; one chiefly whiskey, flavored with acetic ether; 2 others flavored with acetic ether.

“*Gin*. — Extract in 9 samples from 0.74 to 5.13, average 1.84 per cent.; 3 samples colored; 1 sample practically alcohol and water.

“*Pale Ale*. — Salicylic acid present as preservative in 3, absent in 4 samples.

¹ The six samples of cider analyzed were sold as “sweet cider” and contained from 3.6 to 8 per cent. by weight of alcohol. The report says: “It will be seen from the above figures that but little care is taken to prevent the further fermentation of a ‘sweet’ cider, and that the resulting liquor sold under the name ‘sweet’ contains rather more alcohol than the average beer. The practice of checking fermentation by the use of salicylic acid has apparently not extended to cider.”

² See statements regarding furfural in kindred compounds, pp. 325-327 above.

"*Beer*. — Salicylic acid in 5, fusel oil in 1 sample.

"*Cider*. — No preservative, more alcohol than average beer, though sold as 'sweet cider.'"

In how far the results of these inquiries by the New York city and Massachusetts boards represent the quality of alcoholic liquors sold in the United States generally is a matter best understood by manufacturers and experts.

Composition of alcoholic liquors.

Although the number of published analyses of alcoholic liquors is very large, the variation in the composition of different specimens of the same kind are so great that it is not easy to tell what is either the range of variation or the average composition of liquors of a given kind. The figures given here will, however, give a general, if not wholly accurate, idea of the proportions of alcohol and other ingredients in some of the more common alcoholic beverages.¹

Wines. — The term wine is applied primarily to the fermented juice of the grape, but similar products are formed by the fermentations of the juice of other fruits. Thus cider is wine made from the juice of the apple, and perry is in like manner pear wine; currant and blackberry wines are likewise made from juices of the fruits.

The preparation of wine is one of the oldest arts. In the primitive method of preparation, which is still in use in some parts of southern Europe and in Asia, grapes are put in a vat and pressed by simple treading of the feet, or by very simple presses. In the manufacture by more modern methods, the wine presses are more or less elaborate machines. The fresh juice or "must" contains generally from 70 to 85 per cent. of water, from 15 to 25 per cent. of glucose, and very small quantities of proteid

¹ The figures quoted here are taken from various authentic compilations, such as those of König, *Chemie der Nahrungs- und Genussmittel*; Allan, *Commercial Organic Analysis*; Blyth, *Foods, Composition, and Analyses*; Hasal, *Foods, Adulterations, and Methods of Detection*; the bulletins of the Division of Chemistry of the U. S. Department of Agriculture, by Wiley, Crampton, Bigelow, and others; and those of the California Experiment Station, by Hilgard and associates. The figures for American beers are largely from analyses by Englehardt. Various special series of analyses of American liquors, including those by Chittenden and Mendel, have been taken into account.

matters, gum, tannin, coloring matters, organic acids, especially tartaric acid, with corresponding salts and mineral matters. As already explained, the fermentation changes the glucose to alcohols, organic acids, and esters. Aside from the color, which in red wines comes from the skins and seeds, the chief differences between different wines depend upon the quantities of alcohol, sugar, and other so-called extractive matters, acids, tannin, and compound ethers. Ordinary red and white wines, like the most of those made in France and Germany, contain from 6 to 11 per cent. of alcohol, and from 1 to $2\frac{1}{4}$ per cent. of sugar. The sugar and other so-called extractives give "body" to the wine. The quantity of free acid, calculated as equivalent to tartaric acid, ranges from about 0.4 to 0.7 per cent.

The sweet wines, like port from Portugal, sherry from Spain, Marsala from Italy, Tokay from Hungary, contain from 7 to 20 per cent. by weight of alcohol, and from 3 to 25 per cent. of sugar. Part of this alcohol, however, is added in the form of brandy to "fortify" the wine and preserve the sugar from further fermentation. French champagnes generally contain from 8 to 11 per cent. of alcohol. American wines are made in varieties corresponding to the dry red wines or clarets and dry white wines of France and Germany, and the sweet wines, such as ports, sherries, and champagnes. The composition of some of the more common kinds of wine is given in Table 9.

The so-called astringent property of wine is commonly associated with the tannin, of which the red wines contain more than the white wines, though the total quantity is only a small fraction of one per cent. at most. The qualities of the wine which are most prized and which gives it the highest commercial value are the flavor and bouquet. The quantities of esters to which these are due are too small, and their characters are not well enough known to allow their estimation by our present methods of chemical analysis. It should be noted that in Table 9 the so-called free acid is reckoned as acetic acid, though the wines contain more or less of other acids, as tartaric. The total solids or "extract" consist mainly of sugar.

Ciders generally contain from a fraction of 1 per cent. to 8 per cent. of alcohol, and 3 or 4 per cent. of sugar. It is to be noted that the term sweet, as applied to cider, means unfermented or slightly fermented; that is to say, sweet cider is

more or less clarified must, while sweet wines are those which, after fermentation, still contain large proportions of sugar. So-called sweet cider, however, is sometimes well fermented, as shown on page 334.

TABLE 9. — *Composition of Wines and Ciders.*

[Proportions by weight.]

	Alcohol.		Free acid as Tartaric. Average.	Total solids or "extract." Average.	Ash. Average.
	Range.	Average.			
<i>European wines.</i>	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.
French, clarets (König) . . .	6-12	8.0	0.57	2.6	0.25
French, clarets (English analyses)	6-12	10.0	0.60	2.1	0.22
French, white (König) . . .	9-12	10.3	0.66	3.0	0.25
French, white (English analyses)	9-12	10.3	0.48	1.6	0.18
German, Rhine, { red	7-12	8.6	0.58	2.8	0.22
{ white	7-10	8.7	0.68	2.5	0.22
Sweet wines:					
Tokay	7-15	10.0	0.58	20.0	0.32
Marsala	14-24	16.0	0.50	5.3	0.38
Malaga	9-14	12.0	0.55	21.7	0.41
Sherry	16-20	17.5	0.48	4.0	0.38
Port	16-18	17.0	0.40	8.0	0.23
Madeira	15-16	15.4	0.43	5.5	0.35
Champagne	8-11	10.0	0.64	14.6	0.16
<i>American wines.</i>					
Dry, red	6-12	9.0	0.73	2.3	0.23
Dry, white	7-14	9.4	0.68	1.8	0.18
Sweet:					
Port	10-17	13.0	0.65	11.2	0.28
Sherry	13-20	15.5	0.63	4.8	0.27
Sweet catawba	10-15	12.0	0.58	12.0	0.14
Champagne	6-10	8.0	0.73	9.7	0.13
<i>Ciders.</i>			<i>Free acid as malic.</i>		
French, fermented	3.5-5	4.0	0.49	4.1	0.28
French, sweet	1-3	2.0	0.49	6.7	0.28
American, fermented	4-8	5.0	0.40	3.9	0.38
American, sweet	0.2-3.5	1.4	0.40	8.2	0.32

Malt liquors. — The different kinds of beer and ale contain from 1 to 9 per cent. of alcohol and from 3 to 7 per cent. of extract. The latter consists mainly of dextrin and allied compounds, while in wines the extract consists mostly of sugars. The differences between the different kinds of malt liquors are due largely to differences in the kind of malt, and the kind and

amount of material added to supply the bitter taste. For this latter purpose, hops are generally used. Of the different kinds of beer, German weiss beer generally contains less than 3 per cent., the German lager beers from 3 to 5 per cent., English beers, ales, and porters from 4 to 9 per cent. of alcohol. The corresponding American products generally contain somewhat less alcohol. The quantities of extracts range from $2\frac{1}{2}$ to 7 per cent. or thereabouts. The composition of different kinds of beer is shown in Table 10.

TABLE 10. — *Composition of Malt Liquors.*

[Proportions by weight.]

Beers, Ales, etc.	Alcohol.		Total solids or "extract." Average.	Ash Average.
	Range.	Average.		
<i>European.</i>	Per cent.	Per cent.	Per cent.	Per cent.
German weiss beer	1-7	2.7	5.3	0.15
Pilsen lager beer	3-4	3.3	4.2	—
Vienna lager beer	3-5	4.7	5.9	—
Munich lager beer	3-5	4.8	7.1	—
Bavarian beer	2-6	3.6	7.2	0.29
Saxony beer	2-6	2.7	5.8	0.25
English ales and porter	3-7	5.0	6.6	—
<i>American.</i>				
Weiss	1-3	1.7	2.4	0.19
Lager	1-7	3.8	5.9	0.26
Ale	2-9	4.6	5.4	0.31
Porter	2-7	4.5	6.0	0.35

Distilled liquors ; spirits. — The variety of distilled liquors or spirits, as they are otherwise called, though perhaps not so great as that of wines, is still very large. The principal kinds are brandy, rum, gin, schnapps, whiskey, and liqueurs or cordials.

They are obtained by distilling alcohol either from wine or from wort prepared in much the same way as those used for malt liquors. Rye and Indian corn, barley, wheat, oats, and other grains in the raw or malted state, as well as the juice of sugar cane, beet root, and potatoes, are used for the purpose. Genuine brandy, otherwise known as cognac or French brandy, is made from wines. Apple and cherry brandies are made from the products of fermentation of the juice of those fruits. Facti-

tious brandies are made from various kinds of distilled spirits. West India rum is prepared from molasses. Commercial alcohol, whiskey, so-called brandy, schnapps, and gin are made from the seeds of grain and from potatoes. In the preparation of these different kinds of spirit, the wort is fermented as completely as may be, and then distilled. The distillate, when rectified by redistillation without the addition of other materials, is known as alcohol or spirits. All of these distilled products are called ardent spirits, because of the inflammability of their alcohol.

Commercial alcohol. — “Proof spirit” contains by the American standard 42.7 per cent., and by the British standard 49.2 per cent., of alcohol by weight. The ordinary commercial “alcohol” of the U. S. Pharmacopœia contains 91 per cent. of absolute alcohol.

Brandy. — The ordinary brandies from wine contain from 40 to 60, and average 45 per cent. of alcohol. The quantities of fusel oil are very small.

Whiskey is commonly named from the kind of grain used in the manufacture, as rye, corn, etc. The alcoholic liquor produced by the first distillation contains water, ordinary alcohol, fusel oil, and volatile organic acids, and is nearly or quite colorless. It is redistilled and thus rectified to reduce the fusel oil and other ingredients, except ethyl alcohol, to a small amount. The resulting product contains from 40 to 50 per cent. of alcohol or thereabouts by weight. The new whiskey has a somewhat rank, sharp taste and odor. To remove this, and to generate the flavor and so-called bouquet, it is subjected to the aging process, being stored in wooden casks for several years. The fusel oil is in part converted into esters. The liquor becomes more mellow and peculiarly fragrant and acquires a brownish color from the wood. Cheaper grades are prepared with more water and less of other ingredients.

Rum, gin, schnapps, factitious brandies. — These are practically spirits, to some one of which more or less material has been added to give color and flavor. Their composition is extremely variable, but generally they contain rather large proportions of alcohol. It may be added that German schnapps are made largely from potatoes.

Liqueurs and cordials. — These are prepared from distilled

spirits and contain flavoring substances and generally considerable sugar.

Fusel oil in distilled liquors.—The common belief that the most deleterious constituent of distilled liquors is fusel oil has led to frequent determinations of the amount by analysis, but the recorded results are hardly sufficient for reliable averages. The figures for fusel oil in Table 11 are therefore only general indications.¹

TABLE 11.—*Composition of Distilled Liquors.*

[Proportions by weight.]

	Alcohol.		Free acid as acetic. Average.	Fusel oil. Average. ¹	Total solids or "extract." Average.	Ash. Average.
	Range.	Average.				
<i>European.</i>	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.
Alcohol, proof spirit, English	—	49.2	—	—	—	—
Brandy, cognac, genuine, from wine	40-60	47.0	0.04	0.10	0.9	0.12
Brandy, from spirits	36-42	39.0	0.01	0.01	0.2	—
Gin	20-40	30.0	—	—	5.5	—
Rum	40-80	60.0	0.10	0.07	0.5	0.05
Whiskey	36-43	40.0	0.03	0.2	—	—
Schnapps, German	—	38.0	—	—	—	—
Liqueurs:						
Bénédictine	—	38.0	—	—	36.0	0.40
Chartreuse	—	32.0	—	—	36.1	—
Curaçoa	—	42.0	—	—	28.6	0.40
Absinthe	—	51.0	—	—	0.5	—
Swedish punch	16-22	19.0	—	—	36.7	0.02
<i>American.</i>						
Alcohol, proof spirit	—	42.7 ²	—	—	—	—
Alcohol, ordinary, U. S. P.	—	91.0	—	—	—	—
Brandy from wine	—	45.0	0.10	—	0.13	—
Rum	—	—	—	—	—	—
Whiskey, genuine	41-45	43.0	—	0.30	0.7	0.01
Whiskey, inferior grades. ³	25-43	35.0	—	0.10	0.4	0.01

¹ From insufficient data; see page 331.² Fifty per cent. by volume.³ As sold in New York city; see page 330.

Root beer and other beverages containing small quantities of alcohol.—By dissolving a small quantity of sugar in water and adding various flavoring materials and yeast to cause fermentation, products are formed which are popularly known under the name of root beer, and contain very small percentages of alcohol. A variety of drinks with similar percentages of alco-

¹ See also statements regarding furfural and other aldehydes on pages 326 and 327 above, and on pages 11-13 and 25-30 of report by Dr. Abel in the present volume.

hol are sold under different names. The data for judging the amounts of alcohol in such beverages are lacking.

Alcoholic preparations from milk: koumiss; kefir; matzoon. The preparation of koumiss by the fermentation of mare's milk was practiced by the Scythians in the time of Herodotus, and has long been customary in Asiatic countries. The milk of camels and asses is treated in similar manner as is cow's milk, to which cane or milk sugar is added. In the Caucasus a material called kefir, and containing several ferments, is used with milk in preparation of a beverage similar to koumiss, but called kefir. In Russia and Siberia these fermented milks have long been common as beverages and more lately the use of cow's milk in this way has extended to Europe and the United States. According to König, the alcohol in koumiss from mare's milk varies from 0.15 to 3.3 and averages 1.9 per cent.; that in Russian koumiss from milk of different kinds, including especially cow's milk, averages 1.1 per cent.; and that of kefir (milk) 0.75 per cent. A sample of koumiss and one of a supposedly similar preparation called matzoon purchased in New York city gave 0.52 and 0.81 per cent. of alcohol respectively.

Alcoholic beverages compared with ordinary food materials.

Table 12 gives the average amounts of nutrients and water in some of the more common food materials and likewise the amounts of alcohol and so-called extractives and other ingredients in alcoholic beverages. In such food materials as meat, fish, eggs, etc., which contain bones, shells, and other inedible constituents, the figures for percentages are those of edible portion freed from the inedible portion or refuse. The nutrients of the edible portion are not wholly utilized by the body. A small portion escapes digestion and is excreted by the intestines along with certain residues from the digestive juices. This is called undigestible or unavailable. The rest, the digestible or available portion, makes generally from 85 to 98 per cent. of the individual ingredients, and on the average about 95 per cent. of the total nutrients of the food.

Of the alcohol in ordinary alcoholic beverages it is estimated that on the average 2% escapes oxidation and that 98% is available. The fuel values are computed by use of the figures on page 306 above. In the computation it is assumed that the so-

called extractives, which consist mainly of sugar and other carbohydrates, have the same fuel value per gram as sugar.

TABLE 12. — *Composition of ordinary food materials and alcoholic beverages.*

Material.	Water.	Unavailable nutrients.	Available nutrients.					
			Protein.	Fat.	Carbo-hydrates.	Ash.	Fuel value.	
							Per pound.	Per kilo.
<i>Ordinary food materials.</i>	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Cal.	Cal.
Beef, round	65.5	1.6	19.7	12.9	-	0.8	950	2090
Beef, sirloin	60.6	1.8	17.9	19.2	-	0.8	1185	2610
Mutton, leg	62.8	1.7	17.9	17.1	-	0.8	1095	2410
Pork, salt fat	7.9	5.4	1.8	81.9	-	2.9	3555	7840
Pork, ham	40.3	3.6	15.8	36.9	-	3.6	1905	4200
Codfish, fresh	82.6	0.8	16.0	0.4	-	0.9	335	740
Mackerel, fresh	73.4	1.3	18.1	6.7	-	0.9	650	1430
Oysters	88.3	0.6	5.8	1.2	3.3	0.8	240	530
Eggs	73.7	1.1	14.4	10.0	-	0.8	725	1600
Cows' milk	87.0	0.5	3.2	3.8	5.0	0.5	300	665
Cheese	34.2	3.4	25.1	32.0	2.4	2.9	1880	4145
Butter	11.0	4.9	1.0	80.8	-	2.3	3410	7515
Wheat bread	35.3	2.9	7.8	1.2	52.0	0.8	1200	2640
Wheat flour	12.0	3.4	9.7	0.9	73.6	0.4	1635	3600
Cornmeal	12.5	3.3	7.8	1.7	73.9	0.8	1640	3610
Rolled oats	7.8	5.1	14.2	6.6	64.9	1.4	1800	3970
Beans	12.6	7.9	17.5	1.6	57.8	2.6	1520	3350
Rice	12.3	2.9	6.8	0.3	77.4	0.3	1625	3580
Potatoes	78.3	1.5	1.8	0.1	17.5	0.8	370	815
Apples	84.6	0.9	0.3	0.5	13.5	0.2	260	570
Sugar	-	2.0	-	-	98.0	-	1755	3870
<i>Alcoholic beverages.</i>				Alcohol.	Extrac-tives. ¹			
Beer, German lager . . .	89.0	0.2	-	4.5	6.0	0.2	250	555
Beer, English ales and porter	88.0	0.2	-	5.0	6.5	-	275	610
Beer, American lager . .	89.0	0.2	-	3.5	6.0	0.3	220	485
Beer, American ales and porter	89.0	0.2	-	4.5	6.0	0.3	250	555
Wines, claret and white .	87.0	0.2	-	9.0	2.5	0.3	335	735
Wine, champagne	77.0	0.4	-	10.0	12.0	-	535	1180
Wine, sherry, port, mar-sala	77.0	0.4	-	16.0	6.0	0.3	620	1370
Chartreuse	21.0	1.6	-	31.0	35.0	-	1620	3570
Brandy, cognac	52.0	1.0	-	46.0	-	0.1	1475	3250
Gin	44.0	0.7	-	30.0	5.0	-	1050	2320
Whiskey, European . . .	59.0	0.8	-	39.0	-	-	1250	2760
Whiskey, American, genuine	56.0	0.9	-	42.0	-	-	1345	2970
Whiskey, American, inferior	64.0	0.7	-	34.0	-	-	1090	2405

¹ Largely dextrin, etc., in beers, and sugar in wines.

The figures in the table for the fuel values of alcoholic beverages as compared with those of ordinary food materials would, if taken by themselves, be deceptive, because they compare only the action of alcohol as food or as fuel for the body with the corresponding action of ordinary food materials, and leave out of account the action of the alcohol as drug, which is not exerted

by ordinary food. When alcohol is taken in excessive quantities its action as drug may far more than counterbalance its nutritive effect. Taken habitually in excess it is ruinous to both health and character.

It is to be remembered furthermore that the occasions when alcohol renders a necessary service as food are exceptional. At best it is a very expensive source of nutriment. For people in health it is unnecessary. The moderate use often leads to excess. In the judgment of the writer, its place as nutriment is where the user is unable, because of either debility or disease, to otherwise obtain fitting and sufficient nourishment from ordinary food materials. The reason for emphasizing these facts is that any statement which compares the nutritive value of alcohol with that of ordinary food is in danger of being used, by interested persons or those who are inclined to self-indulgence, without the qualification needed to make up the whole truth.

CHAPTER VI.

THE USE OF "TEMPERANCE DRINKS."

H. P. BOWDITCH, M. D.

SOME years since the Massachusetts State Board of Health, in connection with the work of Food and Drug Inspection, caused an analysis to be made of a number of proprietary medicines belonging to the class of tonics and bitters. The results of this investigation were published by the Board in its 28th Annual Report (1896), p. 615, showing that in the beverages thus examined the amount of alcohol varied from 6 to 47.5 per cent. by volume. As some of them have been recommended as temperance drinks it seemed desirable in connection with the present study of the liquor problem to obtain as definite information as possible with regard to the actual use of these drinks. Absolutely accurate statistics were not, of course, to be expected, but it was thought that the statements of retail druggists as to the demand for the various beverages in their respective communities would furnish trustworthy evidence upon this subject.

Mr. A. C. Robertson, a commercial traveler, whose business brought him into relation with the principal representatives of the drug trade in New England, was, therefore, requested to inquire into and report upon this question. The following report, presented by him, includes a table showing, in the first and second columns, the amount of alcohol contained in forty-two of the tonics and bitters examined by the Massachusetts State Board of Health, and, in the following columns, the sales of these beverages in each of the six New England States. The meaning to be attached to the words "large," "small," "fair," etc., is explained by Mr. Robertson in his report. Under the name of each State is indicated the character of the state law regulating the sale of liquor, and it is interesting to observe that, where any difference is to be noted in the sale of any beverage in the various States, the difference is, almost without exception,

in favor of those States having prohibitory liquor laws. The conclusion which Mr. Robertson draws in his report seems therefore to be entirely justified.

The dose recommended upon the labels of the preparations examined varied from a teaspoonful to a wineglassful, and the frequency also varied from one to four times a day, "increased as needed." It will also be noted that the proportions of alcohol given in the medicines quoted vary from those in the stronger ales and beers to those in the weaker whiskeys and brandies.

Statistics regarding the use of compound and proprietary medicines, bitters, temperance drinks, etc., in the New England States for the year 1899, prepared by Mr. A. C. Robertson, for the Committee of Fifty.

The following table shows for each form of medicine, drink, etc., the percentage of alcohol per volume contained in it, and the sale in each of the New England States. The figures are derived from an inquiry made among the wholesale and retail druggists. The number of retail druggists in New England is estimated to be: Maine, 390; New Hampshire, 230; Vermont, 225; Massachusetts, 1500; Rhode Island, 235; and Connecticut, 450.

The average yearly sale for each druggist is classed as follows: over 200 bottles, very large sale; from 100 to 125, large sale; from 70 to 90, good sale; from 36 to 60, fair sale; less than 20, small sale. From these figures it would appear that at least 300,000 bottles of Ayer's Sarsaparilla are sold annually in Massachusetts, and as this contains 26.2 per cent. of alcohol, it is clear that many people are partaking pretty freely of an alcoholic drink without, perhaps, being aware of it. A comparison of the amount of alcohol contained in these so-called non-alcoholic drinks with that sold as alcoholic drinks throughout New England would be interesting and instructive, but it is not possible to obtain the data. It is clear that very large quantities of drinks containing a greater percentage of alcohol than the ordinary wines and beers are consumed among the most rigorous of total abstinence circles, and one of the foremost advocates of total abstinence has permitted her picture to be used as an advertisement of one of the most alcoholic of these drinks.

TABLE 13.

Name.	Percentage of Alcohol.		Maine. Prohibition.	New Hamp- shire. Prohibition.	Vermont. Prohibition.	Massachu- setts. License and local option.	Rhode Island. License and local option.	Connecti- cut. License and local option.
	By volume.	By weight.						
Howe's Arabian Tonic, "not a rum drink"	13.2	11.1	Small.	Small.	Small.	None.	None.	None.
Liebig Company's Cocoa Beef Tonic	23.2	19.2	Good.	Good.	Good.	Good.	Small.	Small.
Mensman's Peptonized Beef Tonic	16.5	13.5	Small.	Small.	Small.	None.	None.	None.
Schenck's Seaweed Tonic, "entirely harmless"	19.5	16.2	Large.	Large.	Large.	Large.	Large.	Large.
Atwood's Quinine Tonic Bitters	29.2	24.2	Good.	Good.	Good.	Good.	Small.	Small.
L. T. Atwood's Jaundice Bitters	22.3	18.3	Large.	Large.	Large.	Good.	Good.	Good.
Moses Atwood's Jaundice Bitters	17.1	14.1	Large.	Large.	Large.	Good.	Good.	Good.
Baxter's Maudrake Bitters	16.5	13.5	Large.	Large.	Large.	Good.	Good.	Large.
Boker's Stomach Bitters	42.6	35.6	Large.	Large.	Large.	Large.	Large.	Large.
Burdock Blood Bitters	25.2	20.9	Large.	Large.	Large.	Large.	Large.	Large.
Carler's Scotch Bitters	17.6	14.6	Small.	Small.	Small.	Small.	Small.	None.
Drake's Plantation Bitters	33.2	27.6	Fair.	Fair.	Fair.	Fair.	Small.	Small.
Flint's Quaker Bitters	21.4	17.4	Fair.	Fair.	Fair.	Fair.	Small.	Small.
Goodhue's Bitters	16.1	13.1	Slow.	Slow.	Slow.	Slow.	Slow.	None.
Greene's Nervura	17.2	14.2	Very large.	Very large.	Very large.	Very large.	Very large.	Very large.
Hartshorn's Bitters	22.2	18.2	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Hoodland's German Bitters, "entirely vegetable and free from alcoholic stimulant"	25.6	21.1	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Hop Bitters	12.0	10.0	Good.	Good.	Good.	Good.	Fair.	Fair.
Hosletter's Stomach Bitters	44.3	37.3	Good.	Good.	Good.	Good.	Good.	Good.
Kaufman's Sulphur Bitters, "contains no alcohol"	20.5	16.7	Large.	Large.	Large.	Large.	Large.	Large.
Liverpool's Mexican Tonic Bitters	22.4	18.4	Slow.	Slow.	Slow.	Slow.	None.	None.
Faine's Celery Compound	21.0	17.0	Very large.	Very large.	Very large.	Very large.	Very large.	Very large.
Pierce's Indian Restorative Bitters	6.1	5.1	Fair.	Fair.	Fair.	Fair.	Small.	Small.
Puritana	22.0	18.0	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Z. Porter's Stomach Bitters	27.9	22.9	Slow.	Slow.	Slow.	Slow.	None.	None.
Pulmonine	16.0	13.0	Large.	Large.	Large.	Very large.	Fair.	Fair.
Rush's Bitters	35.0	29.0	Good.	Good.	Good.	Good.	Slow.	Slow.
Richardson's Concentrated Sherry Wine Bitters.	47.5	40.4	Good.	Good.	Good.	Good.	Fair.	Fair.
Job Sweet's Strengthening Bitters	29.0	24.0	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Thurston's Old Continental Bitters	11.4	9.4	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Warner's Sate Tonic Bitters.	33.7	29.7	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Warren's Bilious Bitters	17.5	14.5	Good.	Good.	Good.	Good.	Slow.	Slow.
Dr. Williams' Vegetable Jaundice Bitters	18.5	15.5	Good.	Good.	Good.	Good.	Fair.	Fair.

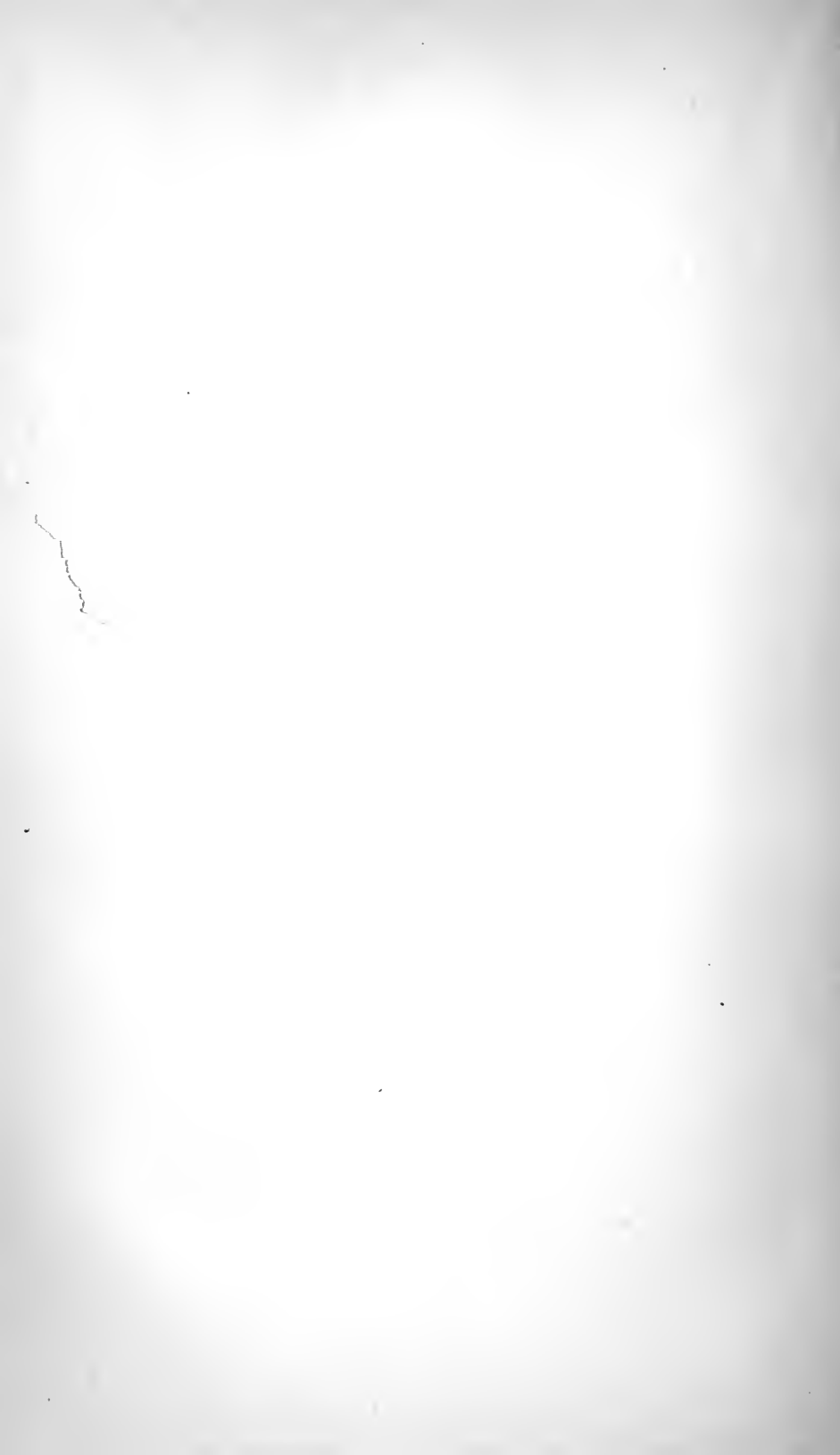
TABLE 13. — *Continued.*

Name.	Percentage of Alcohol.		Maine, Prohibition.	New Hampshire, Prohibition.	Vermont, Prohibition.	Massachusetts, License and local option.	Rhode Island, License and local option.	Connecticut, License and local option.
	By volume.	By weight.						
Golden's Lij. Beef Tonic, "recommended for treatment of alcohol habit"								
Ayer's Sarsaparilla	26.5	21.7	Large.	Large.	Large.	Large.	Large.	Large.
Hood's Sarsaparilla	26.2	21.5	Very large.	Very large.	Very large.	Very large.	Very large.	Very large.
Allen's Sarsaparilla	18.8	15.8	Very large.	Very large.	Very large.	Very large.	Very large.	Very large.
Dana's Sarsaparilla	13.5	11.2	Slow.	Slow.	Slow.	Slow.	Slow.	Slow.
Brown's Sarsaparilla	13.5	11.2	Fair.	Fair.	Fair.	Fair.	Fair.	Fair.
Carbutt's Sarsaparilla	13.5	11.2	Fair.	Fair.	Fair.	Slow.	Slow.	Slow.
Radway's Resolvent	8.8	7.1	Good.	Good.	Good.	Good.	Fair.	Fair.
Beet Tonic	7.9	6.5	Large.	Large.	Large.	Large.	Large.	Large.
	7.6	6.3	Very large.	Very large.	Very large.	Very large.	Very large.	Very large.

THE PATHOLOGICAL EFFECTS OF ALCOHOL.

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THE PATHOLOGICAL EFFECTS OF ALCOHOL.

Introduction. — In considering the action of alcohol upon the living body, it is convenient and customary to distinguish between the physiological, the pharmacological, and the pathological action or effects of this agent, although in a broad sense all marked deviations from the normal condition produced by alcohol are pathological. Inasmuch as previous articles in this book have treated of the composition and relative toxicity of the constituents of alcoholic beverages, and of the action of alcohol on the digestion, the circulation, the respiration, and the nervous and muscular activities, this article is intended to be a concise statement of the pathological effects of alcohol and of alcoholic drinks in the more restricted sense of the term “pathological,” and especially of those effects which are characterized by demonstrable anatomical changes in the body.

It may at the outset be stated that the injurious effects of alcohol upon the body are represented only in part by known anatomical lesions, for we are still ignorant of the anatomical basis of many of the morbid manifestations produced by this substance. With improvements in methods of microscopical investigation our knowledge in this respect has materially increased, and from still more refined methods further advance in the same direction may be expected.

The questions of primary importance concerning the effects of alcoholic beverages relate to the action of ethyl alcohol, which is the chief harmful constituent of such drinks, although the effects of other possible ingredients, such as the flavoring essences and the higher alcohols, and the influence of concentration of the alcohol are by no means to be ignored. In this article, by the word “alcohol,” unless otherwise specified, ethyl alcohol is to be understood.

Our sources of information concerning the morbid effects of

alcohol are experiments upon animals and observations upon human beings. The experimental method has the advantages that the conditions can be better controlled and are less complicated, and the results, therefore, are generally clearer of interpretation than in the case of observations on human beings, but great caution should be exercised in applying directly to human beings the conclusions derived from animal experiments.

I. RESULTS OF EXPERIMENTAL INVESTIGATIONS.

Alcohol in sufficient quantities is a poison to all living organisms, both animal and vegetable. Our chief interest in this connection is with those experimental results which shed light upon the pathological-anatomical effects of alcoholic drinks upon human beings. During the last fifty years many experiments to elucidate this subject have been made upon animals, most frequently upon rabbits, dogs, and swine. Different sorts of alcohol and of alcoholic drinks in varying doses and for varying lengths of time have been administered to animals in different ways, the best and most commonly employed method being injection into the stomach through a soft rubber tube passed down the gullet.

An elaborate experimental investigation, extending over four years, of the pathological effects of alcohol upon rabbits has been made in behalf of the Physiological Sub-Committee of the Committee of Fifty by Dr. Julius Friedenwald in the Pathological Laboratory of the Johns Hopkins University and Hospital. Reference will be made to conclusions derived from these experiments, which have hitherto been published only in part.

The symptoms of acute alcoholic intoxication in the animals named resemble so closely those in human beings that the experimental method would seem adapted for the study of anatomical changes which may be produced under these circumstances. On the other hand, most experimenters record unsatisfactory, although not wholly negative, results in their attempts to reproduce experimentally the characteristic symptoms and lesions of chronic alcoholism as observed in human beings.

Experimental Acute Alcoholic Intoxication. — Inasmuch as the symptoms of acute alcoholic intoxication in animals, as well

as in man, are referable almost entirely to the nervous system, it is not surprising to learn that the only significant anatomical changes produced by this condition are of the nerve cells and their processes. Hyperæmia of the stomach with increased secretion of mucus is also often present, especially when the alcohol is given in a concentrated form. The nervous changes are of such a nature that they can be detected only by the delicate modern methods introduced by Golgi, Nissl, and Marchi for the study of the microscopical characters of the nervous system, and hence our knowledge concerning them dates back scarcely a decade. Berkley's paper published in 1895 and preceded only by the brief articles of Vas. in 1894, and of Dehio in 1895, which were based upon examination of a small material, is the first systematic and elaborate study by modern methods of the changes of the central nervous system in experimental acute and chronic alcoholic intoxication. Dr. Berkley's examinations were made, in behalf of the Committee of Fifty, upon the brains and spinal cords of rabbits used in Dr. Friedenwald's experiments. Another valuable investigation of the influence of acute alcoholic poisoning on nerve cells is that conducted under Dr. Hodge's direction for the Committee of Fifty by Colin Stewart, and published in 1896. Among later investigators of this subject may be mentioned Marinesco (1897), Jaccotet (1897), Carrara (1898), H. Braun (1899), and Kleefeld (1901).

Two different kinds of lesion of the nerve cells have been found in acute poisoning of animals by alcohol, the one, revealed by the Golgi method, being of the cellular processes, and the other, shown by Nissl's stain, being of the body of the cells. The former, described as "the moniliform change," is characterized by the appearance of irregular swellings or varicosities in the course of the protoplasmic processes of some of the nerve cells, associated with partial loss of the delicate bud-like or spinous projections normally present on these processes. The other change, designated "chromatolysis," is the disintegration of the small, stainable granules, known as the Nissl bodies, which can be demonstrated by certain methods of hardening and staining within normal nerve cells. It is not within the scope of this article to describe the finer histological details of these lesions.

The extent and the intensity of these changes in the nerve cells depend upon the depth of the alcoholic intoxication. Nerve cells altered in the ways described have been found in the cerebral hemispheres, the cerebellum, the medulla oblongata, the spinal cord, and the sympathetic ganglia, but even in extreme degrees of the lesions it is only a minority of the cells which are affected. Kleefeld claims that the moniliform change occurs almost instantaneously, and may be found within a few minutes after the entrance of toxic doses of alcohol into the circulation. Stewart found beginning chromatolysis in nerve cells of a cat killed in fifty minutes by the injection of a large dose of alcohol into the abdominal cavity. The most extensive changes have been found in animals subjected to repeated, profound intoxication.

There is considerable difference of opinion concerning the interpretation of these changes and their relation to the symptoms of alcoholic intoxication, but the weight of evidence favors the view that they cannot be satisfactorily utilized to explain the symptoms. The same changes occur from various causes and under a great variety of conditions which have nothing in common with the phenomena of alcoholic intoxication. They do not represent any serious or permanent damage to the nerve cells, but are readily recovered from after disappearance of the causative factor. It has even been questioned whether these changes are really of a degenerative nature, some authors being inclined to refer them to abnormal movements of protoplasm or other manifestations of cell life.

Experimental Chronic Alcoholism.— Since the publication in 1851 of the important work by Magnus Huss on chronic alcoholism many experiments have been made to determine the effects upon animals of the long-continued use of alcohol. The most extensive and prolonged series of experiments of this nature hitherto made is that for the Committee of Fifty by Dr. Friedenwald in the pathological laboratory of the Johns Hopkins University and Hospital. The details of these experiments will be published elsewhere. Most of the one hundred and twenty rabbits used in these experiments received daily, through a soft rubber stomach tube, from five to eight cubic centimetres of alcohol largely diluted. These quantities sufficed to induce within half an hour a drunken stupor which lasted from three

to five hours, the animal generally appearing well on the following day.

Dr. Friedenwald observed, as other experimenters have done, marked individual variations in susceptibility to the injurious effects of the continued use of alcohol. While the tolerance of any given animal could not be positively foretold, young rabbits, pregnant females, and those weighing under one thousand grammes were the most susceptible. Certain individuals were found to be so resistant that they seemed capable of tolerating daily intoxicating doses of alcohol for an indefinite period. Thus, one rabbit was given alcohol for over four years, receiving in this time over four litres of absolute alcohol without permanent ill effects; others were fed with alcohol for three and a half and for three years. These animals had the best of care and were kept under excellent sanitary conditions. On the other hand, some of the rabbits died from acute intoxication after a few doses, and the majority succumbed after shorter or longer periods of time, with gradual loss of weight and exhaustion. If especial care was taken to lessen or to intermit the dose of alcohol when the animal began to lose weight, it was found possible later to increase the dose and to keep a considerable number of the rabbits alive for an indefinite period. Under favorable conditions the animals tended to gain in weight when taking alcohol, especially during the early period.

As regards the pathological effects, there have been considerable differences between the results reported by various experimenters. Some of the earlier experimenters found practically no anatomical changes in animals to which intoxicating doses of alcohol had been fed for weeks or months. The experiments of Dujardin-Beaumetz and Audigé (1879-1884) on swine, extending over three years, which are among the most elaborate and painstaking investigations of this subject ever made, yielded practically negative results, so far as pathological lesions are concerned. On the other hand, the more recent experimental researches, although not altogether in accord, have in general been more fruitful in positive results.

While these discrepancies are at present partly inexplicable, some at least may be accounted for by differences in the animals selected for experimentation, by variations in the quantity, quality, and mode of administration of the alcohol, by the

duration of the experiments, by the technique employed in the microscopical examinations, and by the concentration of attention upon changes in special organs.

It is to be noted that in most of the experiments the amount of alcohol given at a single dose sufficed to produce marked symptoms of intoxication, this quantity being in ratio to the body weight generally much greater than that taken by heavy drinkers. No systematic experiments have been made to determine the pathological effects upon animals of the long-continued use of alcohol in quantities so small as to produce no manifest symptoms of intoxication; but in view of the comparatively meagre results in the experiments with moderately intoxicating doses, it seems improbable that experiments of the former character would yield positive results.

Naturally the attention of the experimenters has been drawn mainly to the examination of those organs which are known to be most frequently affected in man in cases of chronic alcoholism, namely, the stomach, the liver, the kidneys, the heart and blood-vessels, and the nervous system.

Stomach. — Congestion of the gastric mucous membrane and increased secretion of mucus are among the most common conditions noted by the various experimenters. Hæmorrhages, erosions, and actual ulceration of the stomach have also been repeatedly recorded. Several experimenters have reported degenerative changes in the cells of the gastric tubules and chronic interstitial inflammation of the mucous membrane.

There is evidence that some of these alterations, especially the more profound ones, are attributable to administration of the alcohol in too concentrated a form and sometimes to mechanical injuries inflicted by the stomach tube.

In Friedenwald's experiments on rabbits there was frequently observed during life a gradual reduction in the amount of free hydrochloric acid in the gastric contents. In some cases hyperæmia, increased secretion of mucus, and fatty degeneration of the epithelial cells of the gastric tubules were found, but in many instances, even after the prolonged use of diluted alcohol, the stomach appeared entirely normal, both to the naked eye and under the microscope.

As a rule, no pathological changes were present in the intestine.

Liver. — Inasmuch as the long-continued excessive use of alcoholic drinks is by far the most common and important cause of cirrhosis of the liver in human beings, the attention of experimenters has been directed especially to the condition of this organ in chronic, experimental alcoholic poisoning.

Of the various anatomical changes noted by the different experimenters, fatty metamorphosis of the liver cells is the one most frequently recorded. This change is not usually present in an extreme degree, and it is not generally associated with loss of the cellular nuclei or other evidences of death of cells. It readily disappears after cessation of the administration of alcohol. Hyperæmia of the liver is not uncommon.

Actual necrosis or death of the liver cells, either singly or in groups, occasionally occurs, but this, at least in marked degree, is exceptional.

An increase in the number of lymphoid cells in the interlobular tissue has been found by a minority of the experimenters. It was noticed in varying degree in some of Friedenwald's experiments, but its occurrence was inconstant and rather exceptional.

Genuine cirrhosis of the liver has not been satisfactorily reproduced by the experimental use of alcohol. It was present in one of the rabbits of Friedenwald's early experiments, but as this was an isolated instance of its appearance, it is not certain that it was attributable to the alcohol. The few experimenters who have reported successful results in this regard have probably mistaken mere accumulations of lymphoid cells for early stages of cirrhosis, or have not excluded changes due to accidental infections, particularly from unintended injuries of the stomach. This failure to produce experimentally cirrhosis of the liver by the use of alcohol cannot be attributed in Friedenwald's series to the too short duration of the experiments. It lends support to the opinion held by many, that in human beings alcohol acts only indirectly in leading to cirrhosis of the liver, or that special predisposing or associated conditions must be present in addition to the action of the alcohol.

Kidneys. — Most of the experimenters have not noted serious anatomical changes in the kidneys, but von Kahliden in a careful research lays especial emphasis upon lesions of this organ in dogs. He describes fatty degeneration and necrosis of the

renal epithelium, hyperæmia of the veins and capillaries, hæmorrhages, and transudation of an albuminous fluid, and considers that with longer duration of the experiments a chronic interstitial nephritis would appear as a result of these grave lesions.

Seven of the rabbits in Friedenwald's series of experiments had marked albuminuria, associated in five cases with casts. Fatty degeneration of the epithelium of the convoluted and Henle's tubules was common, although not constant. In a few instances there was necrosis of the epithelium, and atrophy of the glomeruli. On the other hand, a number of the rabbits showed no changes in the kidneys after long-continued use of alcohol. An actual chronic interstitial nephritis was not produced.

Heart, Blood vessels, and Blood. — In Friedenwald's experiments fatty degeneration of the muscle of the heart was found in most of the rabbits which died from chronic alcoholic intoxication, but was absent in those which were killed after cessation of the use of alcohol.

In these experiments, as well as in those of others, now and then a sclerotic or atheromatous patch was found on the inner surface of the aorta or other blood-vessel. This lesion was present, however, too inconstantly to be attributed with any certainty to the action of the alcohol, especially as similar changes occasionally are found in animals which have not received alcohol. Pétrov, however, describes progressive sclerosis of blood-vessels in experimental alcoholism.

Fatty degeneration of the endothelial cells and sometimes of the smooth muscle is found with sufficient frequency in the blood-vessels of different organs to be ascribed to the effect of the alcohol.

Often the distribution of the blood does not differ materially from the normal, but there may be hyperæmia of certain organs, most commonly of the stomach, liver, kidneys, and brain.

Friedenwald noted in many instances a considerable reduction in the percentage of hæmoglobin. In those chronic intoxications which terminated fatally there was usually, during the last month or so of life, a distinct anæmia, with reduction in the number of both red and white corpuscles. Fatty degeneration of leucocytes may occur.

Nervous System. — The more recent experimental studies of

the pathological effects of alcohol have been concerned especially with the condition of the central and the peripheral nervous system. In animals, dead from chronic alcoholic poisoning, changes of the nerve cells have been found identical with those described under "Experimental Acute Alcoholic Intoxication" (p. 353). There is reason to think that these changes belong, even in the chronic cases, to the more immediate, acute effects of alcoholic poisoning, for in Friedenwald's experiments they were often absent in animals which did not die, but were killed in the course of the experiments, and they were not observed in animals allowed to live a few days after the alcohol was stopped.

Of other lesions of the brain and spinal cord ascribed to chronic alcoholism in animals, Afanassijew and Braun describe fatty and vacuolar degeneration of nerve cells; Braun also describes a vacuolar rarefaction of the medullary substance, fatty degeneration of the myelin, and the appearance of fatty granular cells along the blood-vessels, and Berkley alterations in the calibre and walls of the blood-vessels and the peri-vascular lymphatics, and accumulations of leucocytes. Small hæmorrhages are occasionally found. None of these changes is constant. Some of the rabbits of Friedenwald's experiments which were killed after daily intoxication with alcohol for over two years showed practically no lesions of the nervous system.

In view of the importance of peripheral neuritis in the pathology of chronic alcoholism in man, much interest attaches to the observations of Spaink, and later of Braun, who found both in rabbits and in dogs subjected to chronic poisoning with alcohol degenerations of various peripheral nerves. Only in the more chronic cases was this degeneration, which is characterized especially by breaking-up of the myeline, well marked. These experimenters claim to have observed in these animals most of the nervous, muscular, and other symptoms characteristic of chronic alcoholism in man. Further confirmatory investigations are needed before these results can be unhesitatingly accepted, especially as similar extensive changes in the peripheral nerves were not observed in Friedenwald's experiments.

Other Organs. — Although hyperæmia, œdema, hæmorrhages, and actual inflammation of the lungs have been described as results of alcoholism in animals, there is no good reason for

this interpretation. Doubtless in many cases these lesions, when found, were attributable to the accidental escape of alcohol into the windpipe. There is no satisfactory evidence that alcohol, administered by the stomach, acts injuriously upon the lungs of animals. In Friedenwald's rabbits a diffuse, fine deposition of fatty granules in the epithelial and interstitial cells of the testicles was often observed. More profound changes in these organs, even atrophy, induration, and softening, are described by Bouin and Garnier as the result of alcoholic poisoning of white rats for eight to eleven months; but these observations need confirmation before acceptance. The same caution is applicable to Sodokow's statements concerning changes in the ovules and spermatozoa.

Experimental Investigations of the Influence of Alcoholism upon Resistance to Infection.—There have been at least a dozen experimental investigations published concerning the influence of alcohol upon susceptibility to infection, the first extensive series of experiments being that of Dr. Abbott, published in 1896, and made in behalf of the Committee of Fifty. These various experiments are in remarkable accord, nearly all showing that animals intoxicated by alcohol are more susceptible to bacterial infection or to toxins than are normal animals. Roos, however, found no increase in susceptibility to the tubercle bacillus of guinea pigs fed with wine, and Kögler, under Gruber's direction, noted a favorable influence of alcohol upon the survival of animals treated with this agent during the stage of acute collapse produced by intraperitoneal injection of killed cultures of *Bacillus prodigiosus*. Deléarde has found that the process of experimental immunization is unfavorably influenced by alcohol.

These researches furnish an experimental basis for the generally recognized lowering of resistance to many infectious diseases manifested by alcoholic patients. They are not, however, decisive as to the usefulness of alcohol in the treatment of infectious diseases in human beings, for the amount of alcohol used in the experiments proportionately to body weight far surpasses that generally given for therapeutical purposes, and the question is one which must be answered by clinical experience.

In this connection may be mentioned the unfavorable influence of alcohol upon pregnant females observed by Friedenwald

in his experiments. Of twenty pregnant rabbits fed with alcohol seventeen aborted, and of these eight died soon afterward of septicæmia. Nearly all of the young which were born at full term died a few days after birth. Laitinen reports a similar experience with pregnant guinea pigs intoxicated with alcohol.

SUMMARY OF THE PATHOLOGICAL CHANGES IN EXPERIMENTAL ALCOHOLISM.

1. There are no satisfactory experimental data to determine the pathological effects upon animals of alcohol or of alcoholic beverages taken for a long time in quantities which produce no marked symptoms of intoxication. In most of the experiments the amount of alcohol administered at a dose, in proportion to body weight, considerably exceeded that usually taken even by heavy drinkers.

2. Animals exhibit marked individual differences in their susceptibility to the injurious effects of the prolonged administration of intoxicating doses of alcohol. While certain individuals succumb quickly, others may be kept alive under these circumstances for at least four years without presenting any serious anatomical lesions attributable to the alcohol. Between the extremes there are all gradations in susceptibility, young animals and pregnant ones being generally the most susceptible.

3. In acute experimental alcoholism there can be demonstrated certain delicate changes in the nerve cells, which readily disappear after stopping the alcohol.

4. The experimental reproduction in animals of certain of the more characteristic diseases of human beings, attributable to the abuse of alcohol, such as cirrhosis of the liver, chronic Bright's disease, and arterio-sclerosis, has not been satisfactorily attained. The most common pathological condition noted in experimental chronic alcoholism of animals is a fatty metamorphosis affecting especially the cells of the liver, the heart muscle, and the kidneys. This lesion soon disappears after stopping the use of the alcohol. Death or necrosis of limited groups of cells in the liver and kidneys may occur, but is inconstant, and, according to most experimenters, is exceptional. More common is an acute or chronic catarrhal gastritis, but this, too, is often absent or but slight. Changes in the central nervous system, similar

to those in acute alcoholism, as well as certain additional ones, may be present in experimental chronic alcoholism. There may also be degenerations of the peripheral nerves. Hyperæmia and small hæmorrhages may occur, especially in the stomach, the kidneys, and the brain. In view of considerable differences in the results reported by different experimenters, and of many still unsolved problems, additional experiments upon the pathological effects of the long-continued use of alcohol and of alcoholic drinks are needed.

5. Alcoholic intoxication increases the susceptibility of animals to many infections, and influences unfavorably the process of immunization. Pregnant rabbits or guinea pigs repeatedly intoxicated by alcohol are likely to abort, and to die soon afterward from some accidental infection. Many of their young die a few days after birth.

II. ALCOHOL AS A CAUSE OF HUMAN DISEASES.

It is universally recognized that alcoholic intemperance is the direct or the contributory cause of an immense amount of sickness and disability, and of a very large number of deaths, concerning which, for obvious reasons, mortality returns furnish only imperfect and partial statistical information.

According to Vacher the Registrar-General's Reports for England and Wales show during the twenty years from 1881 to 1900 a total of 110,215 deaths due to chronic alcoholism, delirium tremens, and cirrhosis of the liver, these being the only causes of death, registered in the reports, which directly represent the mortality from alcoholic intemperance. These deaths correspond to an average death-rate per million living for the twenty years from these three diseases of 188.45, that among the male population between 226.7, and that among the female population 152.6. A large majority of these deaths occurred between twenty-five and fifty-five years of age, when men and women should be at their best. During the twenty years there was an increase in the mortality from each of these diseases, but only in the case of chronic alcoholism was this very remarkable. The three causes of death included in these statistics by no means represent the total mortality from alcoholic intemperance, for the agency of alcohol in the causation or the fatality of Bright's disease, diseases of the heart and blood-vessels,

apoplexy, paralysis, insanity, pneumonia, tuberculosis, and other diseases is not recorded in these or in most other mortality returns.

For the last twelve years the official mortality reports from the larger Swiss cities contain data concerning alcoholic excess as a contributory as well as a direct cause of death. The statistics (cited from Delbrück) from the fifteen largest Swiss cities for the eight years from 1891 to 1898 show that in 6.4 per cent. of all deaths of persons over twenty years of age alcoholism was either the direct cause or a contributory cause. The percentage is 10 for men over twenty years old. Different places and countries, of course, show marked differences in the mortality from intemperance. Switzerland ranks among countries with a medium consumption of alcohol.

Individual predisposition and also predisposition of special organs of the body are important factors in the etiology and pathology of alcoholism. It is a matter of common experience that many persons drink beer, wine, and spirits in moderation throughout a long life without apparent impairment of the general health. There are, however, others so extremely susceptible to the action of alcohol that they are intoxicated by quantities so small as to be without manifest effect upon most persons. In some individuals, also, the symptoms of intoxication assume an unusual so-called pathological type. Unusual susceptibility to the toxic influence of alcohol, as well as a morbid craving for alcoholic liquors in increasing quantities, have been attributed in many instances to an inherited or acquired degeneracy or instability of the nervous system, but the opinions of authorities are much divided as to the relative importance to be attached to this factor in the causation of alcoholism. The periodical excessive drinking which characterizes dipsomania is now generally regarded as a manifestation of a disease which some physicians consider to be analogous to epilepsy. Of the injurious effects of the continued use of even small quantities of alcoholic liquors upon infants and children Demme and others have brought abundant evidence.

The importance of predisposition is further illustrated by the familiar fact that some persons after a relatively short period of immoderate indulgence in alcoholic liquors present the symptoms and lesions of chronic alcoholism, whereas others under

the same conditions, or perhaps even more intemperate, are affected only after a much longer interval or, it may be, not at all. Evidence of predisposition on the part of organs is furnished by the remarkable differences in the manifestations and the localization of alcoholic diseases in different persons, so that in one the kidney, in another the liver, in another the heart, and in still another the brain is the organ chiefly damaged by alcohol. These differences can be explained only in part by the kind and concentration of the alcoholic beverages used.

There being no constant and definite relation between the amount of alcohol consumed and its pathological effects, it is difficult to make statements which shall be both precise and truthful concerning possible pathological effects of what is ordinarily called "moderate drinking." This subject is one concerning which widely divergent views have been expressed even by those whose opinions are authoritative in medicine. Its scientific investigation encounters peculiar difficulties, and at present the established facts are too few to permit secure, broad generalizations. The increasing recognition, especially within recent years, of the importance of this matter, is sure to lead to more exact knowledge concerning it, but it will probably be a considerable time before an entire agreement of medical opinion in this regard is reached.

A difficulty at the beginning is encountered in attempting to define moderation in drinking. What is moderate for one person may be immoderate for another. The discussion of this fundamental aspect of the subject belongs to the consideration of the physiological and the pharmacological action of alcohol, and has been presented in other articles in this book, particularly in Dr. Abel's "Review of the Pharmacological Action of Ethyl Alcohol." There it has been pointed out that the closer analysis of the physiological effects of alcohol, especially upon the nervous centres, has led many to adopt, in comparison with earlier standards, a considerable reduction in the quantity of alcohol which may be properly designated as "moderate," that is, the quantity which may be habitually taken without bad results of any kind. It may here be said that increased knowledge of the pathological effects upon the body of the continued use of alcoholic beverages has drawn many physicians who have carefully studied the subject to a similar conclusion, the demon-

stration of the causative relation of beer-drinking to diseases of the heart and arteries having been of especial influence upon medical opinion in this regard. Alcoholic diseases are certainly not limited to persons recognized as drunkards. Instances have been reported in increasing number in recent years of the occurrence of diseases of the circulatory, renal, and nervous systems, reasonably or positively attributed to the use of alcoholic liquors, in persons who never became really intoxicated and were regarded by themselves and by others as "moderate drinkers." Strümpell believes that the daily consumption of three to four litres of beer will eventually act injuriously upon the heart. No precise figures are available concerning the frequency with which alcoholic indulgence in its lesser degrees causes disease. It is well established that the general mortality from diseases of the liver, kidney, heart, blood-vessels, and nervous system is much higher in those following occupations which expose them to the temptation of drinking than in others.

The bodily injury inflicted by alcoholic abuse may be entirely latent until it is made manifest by some accessory circumstance. Thus delirium tremens, neuritis, and other nervous manifestations of alcoholism often make their first appearance as an accompaniment or sequel of some acute febrile disease, such as pneumonia, or of traumatism, loss of blood, emotional shocks, or other affection. Or the bad effects of immoderate drinking may be unsuspected until they influence unfavorably the course and outcome of some infectious disease or of a surgical operation.

Alcoholism, as pointed out by Strümpell, represents the summation of injuries inflicted upon the tissues of the body by alcohol, each injury being perhaps minimal in amount but the total constituting serious disease. It is not necessary to consider here the various theories concerning the mode of action of alcohol as a poison, or the extent to which it does injury by acting directly as such upon the cells, or indirectly through nutritive or other disturbances. In one way or another most of the organs and tissues of the body may become the seat of morbid changes attributable to the poisonous action of alcohol. For the purposes of this article it is not necessary to attempt more than a brief specification of the more characteristic and common pathological effects of alcohol. None of the lesions of

either acute or chronic alcoholism is absolutely pathognomonic of this condition, but in many cases of death from chronic alcoholism the anatomical changes in their entirety are sufficiently characteristic to establish a probable diagnosis without knowledge of the history of the case.

The poisonous effects of alcohol may be referred to the following classes of morbid change, which may occur either singly or in combination: (1) disturbances of function, (2) irritative effects marked by hyperæmia, with which may be associated hæmorrhages and transudation of serum, (3) cellular degenerations of various kinds, (4) production of new connective tissue, (5) abnormal metabolism, characterized especially by increased formation of fat or deposit of fat in abnormal situations. When brought directly in a concentrated form into contact with the tissues alcohol is an inflammatory irritant. The most important and characteristic pathological action of alcohol is that of a cellular poison. It is probable that the new growth of fibrous tissue in certain alcoholic diseases, especially in cirrhosis of the liver, is consecutive to a primary degeneration or death of cells, although this opinion is disputed.

In the rare instances of *fatal acute alcoholic poisoning*, when a large quantity of strong spirit is taken at once, no characteristic lesions are found after death. There may be redness and inflammation of the stomach and congestion and hæmorrhages in the brain, the lungs, and perhaps other organs, but these changes are not invariably present, and they are in no way diagnostic. We have experimental evidence, which has already been presented, that acute alcoholic intoxication causes certain changes of a transitory nature in the nerve cells, and similar changes have been found in human beings in the acute cerebral disorders of alcoholism.

CHRONIC ALCOHOLISM. — *Alimentary and Respiratory Tracts.* — Chronic catarrhal inflammation of the stomach is a common affection of alcoholic patients, but the lurid descriptions and pictures of the drunkard's stomach in certain popular or pseudo-scientific "temperance" tracts and books are drawn from the imagination and not from nature. There may also be intestinal catarrh, but usually no marked lesions are found in the intestine, except in cases of cirrhosis of the liver. Catarrh of the pharynx, larynx, and bronchi is common in alcoholic patients.

Liver. — Cirrhosis of the liver, although not the most common, is the most characteristic pathological-anatomical condition produced by alcohol. The liver is hard and nodular, and usually reduced in size, although it may be larger than normal. The microscope shows a new growth of connective tissue between the liver lobules and atrophy of liver cells, which may also be fatty. The immoderate use of alcohol is the cause of probably over ninety per cent. of the cases of hepatic cirrhosis, and some think that it is the sole cause. This disease is the result especially of drinking strong spirits, being rare in beer drinkers, although not so infrequent in France from excessive use of wines. The disease is sometimes called "the gin-drinker's liver." Cirrhosis of the liver was found by Formad in only six of 250 post-mortem examinations on confirmed drunkards who had died suddenly from the effects of alcohol. Although other statistics show a much higher percentage of cases, this disease is upon the whole a relatively infrequent form of chronic alcoholism, except in regions where excessive drinking of strong spirits prevails. Deposition of fat in the liver cells is common in alcoholism, and large fatty livers, as well as cirrhotic livers, are found in drunkards.

Pancreas. — With or without cirrhosis of the liver, chronic interstitial inflammation of the pancreas may be the result of alcoholic intemperance. In eight of thirty cases of this disease studied by Opie there was a history of alcoholic excess, but in three of these cases the affection was only indirectly, if at all, referable to the use of alcohol.

Kidneys. — There has been much discussion concerning the effect of alcohol upon the kidneys. Large hyperæmic kidneys are found with great frequency in those who drink beer to excess, but this is a condition of functional hypertrophy rather than of actual disease, the kidneys being called upon for extra work in eliminating the excessive amount of fluid taken into the circulation. The evidence, however, is strong that alcoholic excess is injurious to the kidneys. The observations of Glaser made in 1891 have since been repeatedly confirmed, that the urine, even after a single alcoholic excess, often contains abnormal elements, such as leucocytes, casts, and crystals of oxalate of lime and of uric acid, indicative of transient irritation or even slight inflammation of the kidneys. The experimental evi-

dence upon this subject furnished by von Kahlden and by Friedenwald has already been cited (p. 357). Although some English authors, following Anstie and Dickinson, deny any causative relation of alcoholic abuse to Bright's disease, Strümpell regards renal disorders as the most common of all the pathological effects of alcohol. The weight of authority and of evidence supports the view that excessive indulgence in alcoholic liquors, fermented as well as distilled, is an important cause of chronic Bright's disease, especially of the small, granular kidney. Strümpell describes also a form of acute nephritis which may rarely result from the long-continued use of alcohol, and occasionally passes into the chronic form.

Heart. — Disorders of the heart are among the most important manifestations of chronic alcoholism, these depending not so much upon any direct injury inflicted upon the heart by alcohol as upon associated conditions resulting from alcoholic abuse. Bollinger and Bauer in Munich were the first prominently to call attention to the frequency of hypertrophied and dilated hearts in those who drink large quantities of beer. This so-called "Munich beer-heart," which is commonly associated with the "beer-kidney," is probably the result mainly of the extra demand upon the heart for work in propelling the excessive volume of fluid in the vessels. The compensation thus established is likely sooner or later to be broken, and then appear serious symptoms referable to cardiac insufficiency. Other causes of hypertrophy of the heart in alcoholic patients are sclerosis of the arteries and chronic Bright's disease. Chronic myocarditis, or new growth of fibrous tissue in the muscle of the heart, although sometimes ascribed to the direct action of alcohol on the heart, is rather the result of disease of the arteries of the heart.

Fatty degeneration of the heart muscle may be caused by alcoholic excess, but a more important condition clinically is the overgrowth of adipose tissue upon the surface and in the substance of the heart, which is found particularly in association with the general obesity of some cases of chronic alcoholism. This latter condition may interfere seriously with the normal action of the heart.

Blood-vessels. — Alcohol is usually regarded, and probably correctly, as one of the causes of sclerosis or atheromatous

degeneration of the arteries, a disease of great clinical importance and attended by varied symptoms and organic lesions according to the particular arteries chiefly affected. In this way alcoholic excess may stand in a causative relation to cerebral disorders, such as apoplexy and paralysis, and also to diseases of the heart and of the kidneys. Dilatation of the veins, particularly about the nose and face, are, together with aene rosacea, familiar manifestations of chronic alcoholism, although they may occur quite independently of this condition.

Nervous System. — The special toxic action of alcohol is, in the first instance, upon the higher nervous centres, a fact which is manifest enough in the familiar symptoms of a drunken fit. Although the special affinity of alcohol for the nervous system has long been known, the most interesting and important clinical and pathological studies of alcoholism in recent years have related to this subject, and have added materially to our knowledge. These researches have shown that the relationship of alcohol to mental disorders and other disturbances of the nervous system is in many instances less simple and direct than was formerly and is still often represented. A problem of fundamental importance, as yet awaiting final solution, is the determination of the part to be assigned to underlying inherited or acquired constitutional defects of the body, chiefly of the nervous system, in the causation and the pathology of the various disorders of the nervous system caused by or associated with alcoholic excess. That this part is a very important one cannot be questioned, but the limits to be assigned to it are at present uncertain. Both the general and the statistical statements current in many medical as well as popular writings upon the causative relation of alcohol to insanity, to epilepsy, and to certain other nervous diseases are often of little value with reference to the question of causation of these diseases in previously normal persons by alcoholic poisoning.

It is important to know that the immoderate drinking of alcoholic liquor may be the first symptom of some disease which, when later recognized, is erroneously ascribed to alcohol as the cause. It is furthermore established that many of the mental and nervous disorders of alcoholism, while they are attributable to the toxic action of alcohol, are dependent in large measure upon an underlying psychopathic constitution, excessive indul-

gence in alcohol rarely producing certain of these disorders in persons of normal constitution. Inebriety in the parents or more remote ancestors ranks among the important causes of this inherited instability of the nervous centres. After making the necessarily large, but not precisely definable allowance for the share of inherited or acquired organic or constitutional defects in the etiology of the nervous manifestations of alcoholism, there still remain cases enough in which alcoholic poisoning is the cause of serious disease of the brain, spinal cord, and nerves in persons of previously normal constitution, so far as can be ascertained.

Much has been done in recent years by psychiatrists in the careful analysis of the precise psychical defects characteristic of the various alcoholic psychoses, and in this way the features particularly distinctive of the mental disturbances due to alcoholic poisoning have been more sharply defined than was formerly the case. Investigations of this nature have been made by Wernicke, Kraepelin, Bonhoeffer, Cramer, and others on delirium tremens, alcoholic neuritis, with the corresponding cerebral and spinal diseases, especially chronic alcoholic delirium or Korsakow's psychosis, acute hallucinatory mania, the "pathological" drunken paroxysm of chronic alcoholics, attended often with acts of violence, and alcoholic epilepsy, but it is not within the scope of this article to attempt a consideration of these interesting results.

Correspondingly sharp anatomical definitions of the various alcoholic diseases of the nervous system are still lacking. The pathological lesions of the brain found with greater or less frequency in cases of chronic alcoholism are thickening, opacity, and adhesions of the membranes, chronic hæmorrhagic pachymeningitis, transudation of serum, atrophy of the cerebral convolutions, a granular condition of the ependyma, atheromatous arteries, and increase of neuroglia in the superficial layers of the cortex. These lesions belong to chronic alcoholism as such rather than to any one of the special alcoholic diseases of the brain. In the acute alcoholic psychoses, of which delirium tremens is the most common and familiar type, the modern histological technique, particularly the Nissl and the Marchi methods, have revealed changes in the nerves and the nerve cells of the brain and spinal cord, but the functional significance of these alterations is not at present well understood.

Since the investigations of Leyden and of Moeli about twenty years ago, alcoholic neuritis has been recognized as an important, although not very common, manifestation of chronic alcoholism. The paralyses, disturbances of sensation, ataxia, and other symptoms of the disease had been previously noted. Recent studies, particularly those of Oppenheim, Gudden, and Cole, have led to the important conclusion that peripheral neuritis is only one part of an affection which may implicate the nerve cells and their processes throughout the whole nervous system. In some cases the peripheral neurones, in others the central neurones are chiefly affected, but the degeneration may affect in a single case various groups of neurones in the brain and in the spinal cord and ganglia, including widely distributed peripheral nerves. The lesion in all cases is primarily a degenerative one. The results of these researches bring into close relationship various alcoholic diseases of the brain, the spinal cord, and the peripheral nerves, especially delirium tremens, Korsakow's psychosis, and multiple neuritis. The underlying condition is a toxæmia induced by alcoholic excess. It is especially in this group of affections that the coöperation of various contributory or exciting causes, such as pneumonia, tuberculosis, or other infection, shock, surgical injury, privation, etc., is most apparent. The patient may have been addicted to alcoholic excess for years, but the introduction of one of these accessory causes suddenly gives rise to the outbreak of one of these disorders of the nervous system.

In this connection may be mentioned various disturbances of vision which are often associated with chronic alcoholism and which are referred by Uhthoff mainly to changes in the optic nerves or their terminations.

The excessive use of absinthe and other cordials and liqueurs is particularly injurious to the nervous centres, for here the flavoring essences in varying degree, as well as the alcohol, are poisonous to the nerve-cells. Epileptic disorders may be caused by the immoderate use of this class of alcoholic liquors.

Disorders of Metabolism. — One of the symptoms of chronic alcoholism, most common in beer-drinkers, is obesity. Adipose tissue may appear in situations where it is not normally present, the most dangerous localization in this regard being between the muscle fibres of the heart. Much of the fine, molecular fat

deposited in the hepatic and other cells is the result of abnormal metabolism of the fats rather than of a true fatty degeneration. An excess of fatty particles in the blood of drunkards has been observed.

The use of alcoholic liquor, especially in the form of the stronger wines, and heavy beer or porter is a well-recognized cause of gouty manifestations in those predisposed by inheritance to this disease.

Strümpell was the first to call attention to the influence of beer in interfering with the oxidation of sugar in the body. He observed in certain cases that the drinking at once of as much as $1\frac{1}{2}$ to 2 litres of beer was followed by a transitory alimentary glycosuria. These observations have since been confirmed and extended. Strümpell recognizes a special form of diabetes mellitus due to alcohol, and he brings the three conditions — obesity, gout, and diabetes — into a group of correlated alcoholic disorders of metabolism.

Lowered Resistance to Disease. — A much larger number of the victims of alcoholic intemperance die of some infectious disease than of the special alcoholic affections. Attention has repeatedly been called in this article to the lowering of the resistance of alcoholic patients to many infectious diseases, and the experimental data bearing upon this point have been summarized. This lowered resistance is manifested both by increased liability to contract the disease and by the greater severity of the disease. Physicians generally recognize the graver prognosis of pneumonia, cholera, erysipelas, and other infections in persons who habitually drink to excess than in others.

The belief was once widely held that those who indulge freely in alcoholic liquors thereby acquire a certain degree of protection from tuberculosis, but this opinion is now completely discredited. Alcoholism, if it does not actually predispose to tuberculosis, as some believe, certainly furnishes no protection against it. The course of tuberculous disease in alcoholic patients is often more rapid than usual.

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